PLEURISY WITH EFFUSION COMPLICATING ARTIFICIAL PNEUMOTHORAX THERAPY WITH SOME OBSERVATIONS ON THE VALUE OF SERIAL BLOOD EXAMINATIONS.

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Acknowledgements.

I have to thank Dr. John Watson, Medical Superintendent of Robroyston Sanatorium, for permission to carry out the work described in this thesis. He has given me much encouragement and helpful advice. I am indebted to Dr. M.A. Foulis, Deputy Medical Superintendent and Senior Resident Surgeon to the Hospital, for many valuable suggestions and criticisms. My thanks are due to Professor J.W.S. Blacklock for his help during the early stages of the bacteriological work.

Finally, I wish to thank the various ward sisters without whose co-operation it would have been impossible to carry out the many clinical examinations and tests employed.

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PLEURISY WITH EFFUSION COMPLICATING ARTIFICIAL PNEUMOTHORAX THERAPY WITH SOME OBSERVATIONS ON THE VALUE OF SERIAL BLOOD EXAMINATIONS.

This thesis was undertaken during the writer's term of office as Senior Resident Medical Officer at Robroyston Sanatorium.

Its objects were:-

(1). To determine the causation of pleural effusions occurring during artificial pneumothorax treatment and to discover the percentage in which tubercle bacilli could be demonstrated.

(2). To note what changes occurred in the erythrocyte sedimentation rate and in the leucocyte count preceding the onset of a pleural effusion, and to note whether or not these changes gave any indication of the type of effusion which might arise.

(3). To observe what changes occurred in the erythrocyte sedimentation rate and leucocyte counts during the course of the effusion, and to note whether any indication of change in the character of the fluid was reflected by changes in the blood.

Fifty patients were studied in detail. As only a percentage of these developed an effusion, the first object was more amply demonstrated by including a further series of twenty-five patients who had developed/

developed fluid during their treatment.

INTRODUCTION.

It would seem pertinent to give first a short review of the history of artificial pneumothorax.

The earliest record of introduction of air into the chest as a therapeutic measure is found in the writings of Hippocrates,who stated that "air may be introduced into the chest through a wound or an incision of the chest wall for empyema." Krause, who unearthed this interesting writing, believed this therapeutic measure was actively practised as early as the fourth century B.C.

There is no evidence that artificial pneumothorax treatment was used during the following two thousand years. About 1774, Bourru of Paris conceived the idea of compressing the lung artificially in pulmonary tuberculosis. It was not until the nineteenth century, namely in 1882, that writings first appeared in England. These came from the pen of James Carson of Liverpool, and to him belongs the credit of observing the phenomenon of lung elasticity with the thorax open. He proposed that cavities could be closed by the introduction of air into the thorax, thus overcoming the elasticity of the lung, and he made several attempts to do this on human subjects/

subjects.

Carson's work was not regarded favourably and it was not until Forlanini of Italy published his results that artificial pneumothorax really came to be recognised as a therapeutic measure. Forlanini introduced nitrogen into the pleural cavity by means of a thin hollow needle. He gave small amounts of gas frequently, treating at first the simple cases, but subsequently he used this technique in severe and complicated cases of pulmonary tuberculosis. About 1890, other writers, including S. Riva-Rocci, Cavallero and Potain, published papers on artificial pneumothorax therapy. John B. Murphy of Chicago developed a technique similar to that of Forlanini, but quite independently, and he published his works about 1898. He hoped not only to close cavities but to cure early cases of pulmonary tuberculosis by artificial pneumothorax. Murphy used much larger amounts of gas - up to 3000 cc., and refilled his patients at intervals of six to ten weeks, introducing the gas by trocar and cannula. Lemke, an associate of Murphy, continued the latter's work until his death in 1906, when this method of treatment fell into disuse in the United States of America for a number of years.

Brauer of Germany revived artificial pneumothorax/

pneumothorax treatment and published his findings in 1906. He differed from Forlanini in that he introduced air through an incision parallel to the ribs. Saugman, a Dane, devised the water manometer in 1907 for measuring intrapleural pressure, thus minimising the danger of the operation. The idea of selective collapse , in contrast to complete collapse, was promulgated separately in the writings of Morgan of England and Ascoli of Germany in 1912.

Between 1909 and 1912 artificial pneumothorax therapy was again used as a form of treatment in pulmonary tuberculosis in the United States of America. Since that time artificial pneumothorax therapy has been used widely throughout the world and in Britain the names of Riviere, Pearson, Burrell, Chandler and Davies are familiar to all who study this subject.

This summary of the history of artificial pneumothorax therapy is taken mainly from the writings of Packard, Hayes and Blanchet, (1).

ANATOMY AND PHYSIOLOGY.

The Anatomy of the Pleura.

The pleura (πλευρα=side of the body or rib) or "innermost skin" of the thorax was first referred to in the English language by Power in 1664. The old anatomists such as Sylvius and Galen had long before described both the pleura and the mediastinum, (Gloyne, (2).).

Each lung is invested by pleura which is in the form of a closed invaginated sac. The portion of it covering the lung surface and lining the fissures between the lobes of the lung is termed the visceral pleura, while that covering the inner aspect of the chest wall, part of the diaphragm, and mediastinum is termed parietal. The visceral and parietal pleurae are continuous with each other around and below the lung root, the double layer below the root being known as the pulmonary ligament. The latter is continuous above with the tube investing the lung root and below it ends in a free falciform border. In health, the visceral and parietal pleurae are in contact, but the potential space between them is called the pleural cavity; it normally contains a small quantity of thin serous fluid. In man, the/

the right and the left pleural sacs do not communicate although they are in contact for a short distance behind the upper half of the body of the sternum. The right pleural sac is wider than the left because of the position of the heart; the upper and lower limits of the sacs are approximately the same on either side, but sometimes the left sac descends to a lower level in the mid-axillary line than does the right.

The Visceral Pleura.

The visceral or pulmonary pleura is inseparably connected with the lung, covering the whole of its surface except where the structures of the lung root enter the lung and along the attachment of the pulmonary ligament.

The Parietal Pleura.

The parietal pleura is one continuous membrane but different portions of it receive characteristic names according to the structure on which they lie.

(1) The costal pleura lines the ribs and the intercostal muscles. Anteriorly, it begins behind the sternum, the line of junction of mediastinal with/

with the costal pleura extending downwards, from the sterno-clavicular joint, and medially, to a point in the midline behind the sternal angle. From this point the costal pleurae descend in contact with each other to the level of the fourth costal cartilage; thereafter they diverge, that on the right side passing down to the posterior surface of the xiphisternal joint. From here it sweeps downwards and backwards behind the seventh costal cartilage, reaches the mid-axillary line at the level of the tenth rib, then ascending slightly, crosses the twelfth and reaches to the level of the spine of the twelfth thoracic vertebra. On the left side the costal pleura diverges laterally at the level of thefourth costal cartilage and descends close to the margin of the sternum to the sixth costal cartilage. Its line then follows the ascending part of the costal cartilage as it passes downwards, the remainder of its course being similar to that on the right side, except that it may extend slightly lower.

(2) The diaphragmatic pleura is continuous above on the outer part of its circumference with the costal pleura along the lines described. Medially, it is continuous with the mediastinal pleura along the/

the line of attachment of the pericardium to the diaphragm. Below, it covers the upper surface of the corresponding side of the diaphragm.

(3) The cervical pleura covers the apex of the lung and is the upward continuation of the costal pleura. It extends upwards from the inner border of the first rib, to the lung apex, its summit reaching the lower edge of the neck of the first rib. From here it descends along the side of the trachea to meet the mediastinal pleura. It is strengthened above by Sibson's Fascia.

(4) The mediastinal pleura forms the lateral boundary of the mediastinum, and above the lung root it is a continuous sheet between the vertebral column and the sternum. It is continuous with the visceral pleura at the lung root, and below, it takes part in the formation of the pulmonary ligament.

In two situations on either side, the lung does not wholly fill the pleural cavity. The first site is between the diaphragm and the inferior border of the lung, the potential space between the pleural layers here, being referred to as the costo-phrenic sinus. The second site lies between the sternum and rib cartilages where the anterior

margin of the lung lies short of the line of pleural reflection; the potential space here is called the costo-mediastinal sinus, (Gray. 3).

Histology.

The pleura is covered on its surface by a single layer of flattened nucleated endothelial cells resting on a basement membrane. Beneath the basement membrane lie networks of yellow elastic and white fibres imbedded in a ground substance containing also connective tissue cells. The elastic fibres run in an irregular network in all directions - longitudinal, transverse and oblique, some being continued to the walls of the sub-pleural lymphatics, (Gray. 3).

The elastic tissue of the visceral pleura surrounds the lung in a network, being connected with two other divisions of the pulmonary elastic tissue,

(1) fibres in the walls of the arteries and veins.

(2) fibres in the walls of the bronchioles.

The unity of the elastic tissue of visceral pleura and lung is important in pulmonary contraction, (Gloyne. 2).

The/

The Blood Supply.

This is derived from aortic intercostal, internal mammary, phrenic, inferior thyroid, thymic, pericardial and bronchial arteries. Three plexuses exist:-

(1) beneath the visceral pleura; this being derived from the bronchial arteries.

(2) beneath the costal pleura; this being derived from the arteries of the thoracic wall.

(3) in the subpleural connective tissue of the mediastinum; this being derived from the bronchial and internal mammary arteries.

The veins correspond closely to the arteries, (Gloyne2).

The Nerve Supply.

These are the intercostal nerves, the phrenic and sympathetic nerves. Capsulated and non-capsulated nerve endings are described in the pleura, (Gloyne 2).

The Lymphatics.

Miller (4), quotes Sappey, who describes the visceral pleural lymphatics as being arranged in the form of irregular polyhedral rings, and he states that "only a single plexus exists in the pleura."

Valves/

Valves are abundant, but as the pleural lymphatics communicate very freely they all readily fill with any injection mass. These valves, however, prevent the injected material from passing into the deep lymphatics of the lung. The pleural lymphatics, on uniting, form several trunks which drain into the hilar lymph nodes, the valves in these trunks pointing towards the hilum. The parietal pleura's lymphatics drain in three directions:-

(1) the costal to the intercostal glands.

(2) the diaphragmatic to the diaphragmatic lymph plexus.

(3) the mediastinal to the posterior mediastinal glands.

Nearly all the parietal pleura's efferent vessels drain into the superior vena cava without first passing through the hilar glands. Gloyne (2), states that this may be of significance in the drainage of fluids from the pleural cavity.

It may be worth noting that a layer of endothelium exists between the lymph vessels and the lymph space in the pleura, this acting as a line of defence, but also as an obstacle to treatment by chemotherapy,(Gloyne 2.).

The Physiology of the Pleura.

All the respiratory movements of the lung affect the pleura. Only two of the latter's surfaces move to any extent, the costal surface and the diaphragmatic surface, (Gloyne 2).

The intrapleural pressure is not properly understood. In health, it varies between -4cm. of water at full expiration, to -10cm. of water at full inspiration, these negative pressures being due largely to the elastic recoil of the lung,(Packard, Hayes and Blanchet,).

In patients with pulmonary tuberculosis in whom artificial pneumothorax therapy is employed, the intrapleural pressure varies considerably and depends on many factors, such as posture, the amount of air in the pleural cavity, and the state of the mediastinum, of the pleura and of the lungs,(1).

Air in the Pleural Cavity.

When air is introduced into the pleural cavity, it changes in volume and in composition. Its volume first increases because body temperature is higher than room temperature and the intrapleural pressure is less than atmospheric pressure generally. Hence new partial pressures are established for the various/

various constituents of the air introduced, and as these differ from the partial pressure of oxygen, nitrogen, and carbon dioxide in the blood, diffusion occurs. Carbon dioxide flows from the blood to the pleural cavity at first. Next, oxygen is absorbed into the blood, and, as this proceeds, the partial pressure of nitrogen in the pleural sac gradually becomes higher than that in the blood and it too passes into the blood stream. This, in turn, leads to a raised partial pressure of oxygen and carbon dioxide in the pleural space and these gases again diffuse into the blood stream. The process will continue till all the air is absorbed. Five hundred cubic centimetres of air can be absorbed completely in one week when the visceral and parietal pleurae are normal, (1).

Fluid in the pleural cavity.

As pleural effusions all have some pathological basis, their causation will not be considered here. The mechanism of their resorption may, however, be discussed now.

The earliest worker who observed the resorptive processes of the pleura was Dybkowsky who, in 1866, injected various substances into the pleural/

pleural cavities in animals, according to Pinner, Moerke and Saley (5). Wright (6) notes that isotonic saline introduced into the pleural sac is quickly absorbed. Ligature of thoracic and right lymph ducts does not affect the rate of absorption from the pleural sac, the fluid absorbed passing chiefly into the blood stream. Proof of this is found if indigo-carmine is dissolved in saline and injected into the pleural sac. It appears in the urine in five minutes but only after half an hour in the thoracic duct. Lymphatic absorption is therefore only of secondary importance.

Leathes and Starling, quoted by Pinner, Moerke and Saley (5), state that the entire mechanism of resorption of isotonic, hypotonic and hypertonic salt solutions can be explained by the assumption that the pleura is a semi-permeable membrane which offers greater resistance to the passage of salts than to that of water. The same authors quote Hamburger, who states that while materials injected into the pleural cavity are being resorbed, there simultaneously occurs an influx of substances from the blood. He also found that an injected fluid

was/

was first changed to isotonicity with blood serum before resorption. Ligation of the thoracic duct did not disturb this process, but ligation of the renal arteries did, on account of the upset in osmotic regulation.

Experiments by Pinner, Moerké and Saley (5), using rabbits, confirmed the observation that the pleura is permeable to the chemical constituents of the blood, this permeability varying for different substances. There is some doubt as to how the fluid in the pleural cavity is absorbed once it has become isotonic with the blood. Leathes and Starling (7) demonstrated that substances in the pleural fluid gradually pass into the blood, but that the solution remains approximately isotonic due to the passage of substances in the reverse direction. The final balanced isotonic solution may be absorbed by the lymphatics according to them. Cohnstein is quoted by Cunningham (8), as expressing the view that after a solution in the peritoneal cavity has reached isotonicity with the blood, it is absorbed because of a small amount of colloidal material in the blood stream which cannot pass out of the latter. Cunningham (8), also quotes Hara who believes that

from/

from his experiments using fluorescein as the dye to be absorbed, the endothelial cells are themselves active. Leathes and Starling (7), however, demonstrated that on introducing sodium fluoride into the pleural cavity to destroy the endothelial cells, no alteration in the rate of absorption of the solution was produced. They thus concluded that the endothelial cells exerted no influence on the absorption.

Cunningham (8) states, in conclusion, that "from the more recent and more exact work, there is a small part of the absorption which takes place from the serous cavities that cannot be explained on the basis of the known laws of osmosis and diffusion."

All these experiments take no account of the alteration in the permeability of the pleura which is chronically inflamed. Accordingly, Pinner, Moerke and Saley (5) undertook a detailed analysis of thirty-two pleural fluids removed from sixteen patients having artificial pneumothorax treatment. Their results indicated that the permeability of the pleura is altered in such cases. During the acute stage of a pleuritis/

pleuritis, pleural permeability is increased from blood to plasma and vice versa. As the duration of a pneumothorax increases, pleural permeability diminishes. These findings are confirmed by those of Mayer, Castaigne, Widal and Rivaut, Ramon and Tourlet, Diest and Scheel. whose experiments they quote. Mayer also noted that substances injected into a tuberculous pleural cavity were absorbed less rapidly than in cases in which a simple effusion was present, this presumably being due to the barrier of fibrin and tuberculous granulation tissue present. All these findings do not explain why a long standing effusion may be resorbed.

These observations on the physiology of pleural effusions will be of interest when the behaviour of effusions developing in the writer's series of cases is subsequently considered.

Description of Methods used in the Investigation of a Patient.

On account of the fact that not a few artificial pneumothoraces are abandoned in the first few weeks following their induction, it was thought advisable to begin the investigation of each patient two or three weeks after the commencement of pneumothorax therapy. By this time, one might be fairly certain whether this particular form of treatment would be continued.

A detailed history of each patient was taken and the clinical findings prior to the induction of the pneumothorax noted. Records were made of all X-ray reports, the films having been read by an expert radiologist. Notes were kept of any ancillary methods of treatment employed. Clinical examination of each patient was carried out every two to three weeks and was supplemented by weekly or fortnightly fluoroscopic examinations. It was unfortunately not found possible to make more frequent fluoroscopic examinations on account of the routine examination of other patients in the hospital. The patients were followed up after discharge, at first, at intervals of one month, and later, at intervals of two months. They were instructed to report back immediately if fluid were discovered at/

at the Tuberculosis Clinic which they attended as out-patients for refills.

Examination of the blood was performed usually at intervals of a fortnight but this varied considerably. If it were thought that a pleural effusion was imminent, weekly blood examinations were the rule. In the later stages of treatment, monthly examinations were performed.

Samples of blood were taken by venepuncture approximately at noon. Two cubic centimetres of blood were withdrawn using only slight pressure to make the arm veins prominent. 1.6ccs. of blood were then mixed in a small tube with 0.4cc. of 3.8% sodium citrate solution. From the remaining 0.4cc. a total white blood cell count was done and blood films were made by the coverslip method. At the initial blood examination, the haemoglobin percentage was estimated using the Sahli instrument, and the total red cell count estimated. The citrated blood was used to estimate the erythrocyte sedimentation rate by the Westergren technique, all the estimations being commenced within two hours of withdrawing the blood. The reading at one hour was observed. Four estimations of the total white cell count were made and the average figure used. From the blood films, which were stained

by/

by Leishman's stain, a differential count of two hundred leucocytes was made. The von Bonsdorff count was also estimated by enumerating the lobes of the nuclei of a hundred polymorphonuclear leucocytes. The Lymphocyte/Monocyte ratio was estimated from the differential count and Houghton's Index calculated from the following formula:-

H.I. = V.B. - (E.S.R.+ (P+M)-2(L+E).).

V.B. = Von Bonsdorff count.

E.S.R.= Erythrocyte Sedimentation Rate reading at one hour.

P = Polymorphonuclear leucocytes.

M = Monocytes.

L = Lymphocytes

E = Eosinophils.

The total number of blood examinations performed was one thousand and sixty-two.

The examination of a pleural effusion was made as soon after its discovery as possible. The fluid was collected in a sterile six ounce bottle containing one ounce of 1.5% sodium citrate solution, previously autoclaved, a few cubic centimetres were collected in a sterile test-tube and the remainder in a clean urine glass. The fluid in the six ounce bottle was centrifuged in sterile centrifuge tubes and from the/

the sediment smears were made. Some were stained by the Ziehl-Neelsen method for tubercle bacilli, while others were stained by Leishman's stain and a differential cell count of two hundred cells was made. If no tubercle bacilli were found on the examination of direct smears, the sediment was treated by the antiformin concentration method and further films prepared. If tubercle bacilli were still not found, a guinea-pig was inoculated subcutaneously with some of the sediment suspended in normal saline. From all the effusions a smear of the sediment was made on Lowenstein's medium for the culture of tubercle bacilli. From the fluid contained in the test-tube a smear was made and stained by Gram's method, a search being made for organisms other than tubercle bacilli. Six platinum loopfuls of the fluid were also transferred into glucose broth and this was incubated for twenty-four hours and then examined for organisms. The fluid in the urine glass was used to estimate the specific gravity by placing an ordinary urinometer in it. The protein content of the fluid was also estimated roughly, by diluting one part of the fluid with nine parts of water and setting up the mixture in an Esbach's albuminometer. The water-fluid mixture was put into the/

the tube up to the mark U and then Esbach's reagent was added up to the mark R. The tube was corked, inverted several times and allowed to stand for twenty-four hours. The reading on the scale was taken as the percentage of protein present, (Gloyne. 2.). Rivalta's test as described by Gloyne (2), was also performed. This consists in adding two drops of glacial acetic acid to one hundred cubic centimetres of water in a tall cylinder and then adding one drop of pleural fluid. When serosamucin, a breakdown product of protein is present, a white cloud follows in the wake of the descending drop of fluid.

Subsequent examinations of the pleural effusion were made at intervals of two to three months and in some patients more frequently.

In order to provide a reasonable number of pleural effusions on which to base conclusions, a series of examinations was made on pleural effusions developing in the course of artificial pneumothorax therapy in twenty-five patients who had no other special investigations carried out. In all, effusions were examined from fifty patients, the total number of fluid examinations being one hundred and twenty-seven.

The Aetiology of Pleural Effusions arising in the course of Artificial Pneumothorax Therapy.

The problem of the aetiology of pleural effusions occurring during artificial pneumothorax therapy has exercised the minds of many workers in sanatoria. A considerable diversity of opinion is found on examining the literature relating to this subject, and it seemed to the writer that a comprehensive clinical and laboratory study of an adequate number of patients would be of value, not only in elucidating the causes of such effusions, but also in guiding the physician in his selection of patients for pneumothorax therapy and his conduct of their treatment.

Accordingly, fifty patients whose pneumothoraces had recently been induced and were likely to be maintained, were selected at random from among the hospital patients, for investigation. As it was obvious that only a proportion of these patients would develop pleural effusions, twenty-five additional patients who had developed effusions during their treatment by artificial pneumothorax were also included in the investigation.

In order to have a standard for the comparison of the patients in this series with those of other workers, the National Tuberculosis Association of

America Classification, as modified by Salkin and Cadden (9) was adopted. The details of the unmodified classification as described by Alexander (10), are given below.

(1) Minimal Lesion.

(a) Slight infiltration without demonstrable excavation.

(b) A small part of one or both lungs - total volume of involvement, regardless of distribution, shall not exceed the equivalent of the volume of lung tissue which lies above the second chrondrosternal junction and the spine of the fourth or body of the fifth thoracic vertebra on one side.

Symptoms.

(1) Slight or none.

(a) Slight or no constitutional symptoms, including particularly gastric or intestinal disturbance or rapid loss of weight, slight or no elevation of temperature or acceleration of pulse at any time during the twenty-four hours.

Expectoration usually small in amount or absent.

Tubercle bacilli may be present or absent.

(2) Moderate.

(b) No marked impairment of function, either local

or/

or constitutional.

(3) Severe

(c) Marked impairment of function, local or constitutional. "Local" means marked dyspnoea on exertion limiting seriously the patient's activities. "Constitutional" means marked weakness, anorexia and tachycardia.

(2) Moderately Advanced Lesion.

One or both lungs may be involved, but the total involvement shall not exceed the following limits:-

(a) Slight disseminated infiltration or fibrosis which may extend through not more than the equivalent of the volume of one lung.

(b) Severe infiltration, with or without fibrosis, which may extend through not more than the equivalent of one third of the volume of one lung.

(c) Any gradation within the above limits.

(d) Total diameter of cavities, if present, should not exceed four centimetres.

Symptoms.

Classified under headings (A), (B), (C) as before.

(3)/

(3) Far Advanced Lesion.

A lesion more extensive than classified under Moderately Advanced or definite evidence of greater cavity formation.

Symptoms.

Classified under headings (A), (B), (C) as before.

Salkin and Cadden's Modification of the Far Advanced group is as follows:-

	I.	II.	III.	IV.	V.
One lung.	Moderate.	Far.	Far.	Far.	Far.
Other lung.	Moderate.	Clear.	Minimal.	Moderate.	Far.

Their sub-division of the minimal and moderately advanced groups was not employed in this investigation. In addition to classifying the present series of patients according to the scheme set out above, the writer has appended, in Table 1, the type of tuberculous disease predominating in each individual patient.

During the course of artificial pneumothorax treatment, several patients developed small collections of fluid in the pleural space, insufficient to cover the diaphragm. These were transitory, did not affect the treatment in any way, and will be considered separately/

separately. Dumarest, quoted by Packard, Hayes and Blanchet (1), believes that they are benign and similar to a "transudate ex vacuo." Accordingly, such patients have been classified under Group X, i.e. those patients in whom no effusion occurred. Group Y includes the patients who developed an effusion while under observation, and Group Z refers to those patients, twenty-five in number, whose pleural effusion was examined in order to supplement the findings obtained from the study of the fifty patients comprising groups X and Y.

It will be of interest to study first the classification of the patients in the three groups referred to in the preceding paragraph. No patient had a minimal lesion, the bulk of patients in Robroyston Sanatorium being advanced in their disease. The symptom grouping according to the scheme outlined, and also the type of disease present, will be recorded in tables 1, 2 and 3. The numbering of the patients is according to the chronological order in which they were studied. Tables 1, 2 and 3 will be found in the following pages.

TABLE I. GROUP X.

No. and Initials.	Sex.	Moderately Advanced.	Far Advanced.
1. H.W.	M.		I.B.Fibrocaseous.
2. W.G.	M.		IV.B.Fibrocaseous.
8. C.McD.	F.		III.C.Caseo-cavernous
11. J.H.	M.	A. Fibrocaseous.	
12. W.J.	M.		III.B.Fibrocavernous.
16. A.B.	F.	B.Caseo-cavernous.	
17. H.G.	M		III.B.Fibrocaseous.
18. R.A.	M.		V.C.Fibrocavernous
19. W.S.	M.	A.Fibrocaseous.	
20.M.McH.	F.		III.B.Caseo-cavernous
21. A.P.	M.		IV.B.Fibrocaseous.
24. M.McA.	F.		I.B.Caseo-cavernous
25. C.C.	F.	B.Fibrocaseous.	
26. E.W.	F.		IV.C.Caseo-cavernous
27. M.B.	F.	B. Caseous.	
28. P.McG.	F.	B. Fibrocaseous.	
30. J.F.	F.	B. Caseo-cavernous.	
33. J.L.	M.		IV B.Caseo-cavernous
37. A.V.	F.		III.B.Caseo-cavernous
38. J.R.	F.		III.B.Caseo-cavernous
41. M.M.	F.		II.C.Caseo-cavernous
46. M.H.	M.		IV.B.Caseo-cavernous
48. W.McM.	F.		I.B.Fibro-caseous.
49. S.M.	F.	B. Caseo-cavernous.	
50. E.R.	F.	B. Caseous.	

TABLE I. GROUP Y.

No. and Initials.	Sex.	Moderately Advanced.	Far Advanced.
3. M.P.	F.	B. Caseo-cavernous.	
4. A.McN.	M.		III.B.Fibrocaseous.
5. C.H.	F.	B. Fibrocaseous.	
6. M.J.	F.		III.B.Caseo-cavernous.
7. A.McI.	F.		IV.C.Caseo-cavernous.
9. M.B.	F.	B. Caseo-cavernous.	
10.M.McA.	F.		III.B.Fibro-cavernous.
13.G.McC.	F.	B.Caseo-cavernous.	
14. E.S.	F.	C.Caseo-cavernous.	
15. E.W.	F.		II.C.Caseo-cavernous.
22. A.L.	F.		II.C.Caseo-cavernous.
23. M.B.	F.		II.C.Caseo-cavernous.
29. J.W.	F.		IV.C.Caseo-cavernous.
31. A.F.	F.		IV.C.Caseo-cavernous.
32. A.K.	F.		IV.C.Caseo-cavernous.
34. A.McN.	M.		II.C.Fibro-cavernous.
35. J.L.	F.		II.C.Caseo-cavernous.
36. D.M.	F.		V.C.Fibro-cavernous.
39. M.F.	F.		IV.C.Fibro-cavernous.
40. M.M.	F.		V.C.Fibrocaseous.
42. M.W.	F.		IV.C.Caseo-cavernous.
43. J.B.	F.		IV.C.Caseo-cavernous.
44. M.T.	F.		IV.C.Caseo-cavernous.
45. M.R.	F.	A.Caseous.	
47. J.B.	F.		IV.C.Caseo-cavernous.

TABLE I. GROUP. Z.

No. and Initials.	Sex.	Moderately Advanced.	Far Advanced.
1. A.L.	F.		IV.B.Fibrocaseous.
2. M.B.	F.		II.C.Caseo-cavernous.
3. S.I.	M.	B. Caseous.	
4. C.C.	F.		III.C.Caseo-cavernous.
5. R.L.	M.		IV.B.Fibrocaseous.
6. A.R.	F.		I.C.Fibrocaseous.
7. C.McK.	F.		IV.C.Caseo-cavernous.
8. J.H.	F.		II.C.Caseo-cavernous.
9. H.McG.	F.	C.Caseo-cavernous.	
10.M.W.	F.		IV.C.Fibro-cavernous.
11.A.H.	F.		IV.B.Fibro-cavernous.
12.I.M.	M.		IV.B.Fibro-cavernous.
13.A.S.	F.		II.C.Caseo-cavernous.
14.R.H.	F.	C.Caseo-cavernous	
15.E.McC.	M.		IV.C.Fibro-cavernous.
16.I.K.	F.		III.C.Fibro-cavernous.
17.M.McM.	F.		IV.C.Fibro-cavernous.
18.M.A.	F.		II.B.Fibro-cavernous.
19.M.A.	F.		III.C.Fibro-cavernous.
20.R.A.	M.		II.B.Caseo-cavernous.
21.J.L.	F.		IV.C.Fibro-caseous.
22.S.S.	F.		IV.C.Caseo-cavernous.
23.M.W.	F.		IV.C.Caseo-cavernous.
24.A.Y.	M.	B.Fibro-caseous.	
25.M.McA.	F.	C.Fibro-cavernous.	

TABLE 2.

CORRELATION OF PATIENT'S CLASSIFICATION.

Symptom Grouping and Type of Disease.

	Group X.		Group Y.		Group Z.	
	No.	%.	No.	%.	No.	%.
Moderately Advanced.	10.	40.	5.	20.	5.	20.
Far Advanced.	15.	60.	20.	80.	20.	80.
Symptom Group A.	3.	12.	0.	0.	0.	0.
B.	18.	72.	8.	32.	8.	32.
C.	4.	16.	17.	68.	17.	68.
TYPE OF DISEASE.						
Caseous.	3.	12.	0.	0.	1.	4.
Caseo-cavernous.	11.	44.	18.	72.	10.	40.
Fibro-caseous.	9.	36.	3.	12.	5.	20.
Fibro-cavernous.	2.	8.	4.	16.	9.	36.

TABLE 3.

SUB-GROUPING OF FAR ADVANCED PATIENTS.

	Group X.		Group Y.		Group Z.	
	No.	%.	No.	%.	No.	%.
Sub-group I.	3.	20.	0.	0.	1.	5.
II.	1.	7.	5.	25.	5.	25.
III.	5.	33.	4.	20.	3.	15.
IV.	5.	33.	9.	45.	11.	55.
V.	1.	7.	2.	10.	0.	0.

In the above tables the percentage is given to the nearest whole number.

It/

It will be seen from Tables 1, 2 and 3 that twenty per cent more patients of both groups Y and Z fall into the far advanced classification than do those patients in Group X, in whom no effusion appeared. Again, fifty-five percent. of patients in Groups Y and Z fall into sub-groups IV and V of Salkin and Gadden's classification, whereas only forty percent. of Group X fall into these sub-groups.

Groups Y and Z manifest a preponderance of patients with symptoms allocating them to symptom-group C, sixty-eight percent., as compared with sixteen percent. for the Group X patients in whom no effusion occurred.

These findings suggest that the farther the disease has advanced in the lungs and the more severe the impairment in function, although these do not necessarily run parallel, as is well seen from Table 1, the more likely is a pleural effusion to complicate artificial pneumothorax therapy. Many authors claim that the more advanced the disease, the more likely is an effusion to follow the institution of a therapeutic pneumothorax; among such workers may be mentioned Davies (11), Weinstein of Davos, quoted by Burrell (12), Parfitt and Crombie (13), Rao (14), Weisman (15), Frimodt-Möller (16) and Nicklas (17).

Packard/

Packard, Hayes and Blanchet (1) state that "the more active and acute the pulmonary lesion the more frequent and the more serious is the pleurisy." From Table 2, it is seen that by adding together the percentages of patients having the more active types of disease, Caseous, Caseo-cavernous and Fibro-caseous, ninety-two per cent. occur in Group X, eighty-four per cent. in Group Y, and sixty-four per cent. in Group Z. It therefore follows that in this series of seventy-five patients, although a high percentage of patients developing a pleural effusion had an active and acute lesion, it is important to realise that many patients with similar lesions did not develop an effusion. This finding does not invalidate the statement quoted but indicates that it is necessary to investigate the more thoroughly other contributory causes in patients developing effusions. Many other workers have brought forward evidence that the liability to effusion varies with the intensity and acuteness of the disease, e.g. Van Muralt and Shortle quoted by Peters and Wooley (18), Goorwitch (19), Nicklas (17), and Naveau quoted by Packard, Hayes and Blanchet (1).

It may be concluded from the evidence presented and from the findings of other workers that the extent and acuteness of the pulmonary lesion have

a/

a considerable influence on the development of a pleural effusion once an artificial pneumothorax is induced. This being so, it might be expected that the degree of pleural involvement, especially by recent tuberculous infiltration, would bear a similar relationship to the incidence of effusions. The means available for assessing pleural involvement are:-

(1) The history in so far as it will indicate the occurrence of previous pleurisy, though the writer recognises that a large number of patients can be found in any sanatorium in whom pleural adhesions are proved to exist and who, in fact, had no positive history of pleurisy; in Table 4 will be found the duration of the patient's history from the onset of illness and from the onset of an ipsilateral pleurisy, should this have occurred.

(2) Skiagrams - if taken soon after the induction of an artificial pneumothorax will show the actual existence of most adhesions.

(3) Thoracoscopy - which experience has shown adds to the findings of the skiagrams, and further, gives visual evidence of the presence of superficial tuberculous nodules.

TABLE 4. GROUP X.

No. and Initials.	Duration of history before induction in months.	Ipsilateral pleurisy. Duration in months between it and induction.
1. H.W.	28.	
2. W.G.	11.	
8. C.McD.	7.	
11.J.H.	7.	
12.W.J.	10.	
16.A.B.	5½.	
17.H.G.	24.	
18.R.A.	24.	
19.W.S.	7.	7.
20.M.McH.	11.	84.
21.A.P.	36.	36.
24.M.McA.	2½.	
25.C.C.	11½.	
26.E.W.	7.	7.
27.M.B.	11.	2.
28.P.McG.	7.	7.
30.J.F.	7.	
33.J.L.	18.	
37.A.V.	5.	2.
38.J.R.	4.	
41.M.M.	5½.	½.
46.M.H.	12.	12.
48.W.McM.	18.	
49.S.M.	3½.	3½.
50.E.R.	5½.	4.

TABLE 4. GROUP Y.

No. and Initials.	Duration of history before induction in months.	Ipsilateral pleurisy. Duration in months between it and induction.
3. M.P.	9.	9.
4. A.McN	6.	
5. C.H.	9.	
6. M.J.	5.	5.
7. A.McI	12.	1½.
9. M.B.	4.	1.
10. M.McA	30.	5.
13. G.McC	12.	
14. E.S.	10.	10.
15. E.W.	12.	3.
22. A.L.	5.	
23. M.B.	7.	
29. J.W.	18.	6.
31. A.F.	5.	3.
32. A.K.	6.	
34. A.McN	7.	7.
35. J.L.	2.	2.
36. D.M.	33.	17.
39. M.F.	4.	
40. M.M.	12.	
42. M.W.	10.	
43. J.B.	11.	60.
44. M.T.	14.	
45. M.R.	3.	
47. J.B.	7.	

TABLE 4. GROUP Z.

No. and Initials.	Duration of history before induction in months.	Ipsilateral pleurisy. Duration in months between it and induction.
1. A.L.	3.	
2. M.B.	6.	6.
3. S.I.	2.	2.
4. C.C.	2.	2.
5. R.L.	24.	
6. A.R.	10.	
7. C.McK	10.	
8. J.H.	½.	
9. H.McG	10.	
10. M.W.	4½.	1½.
11. A.H.	7.	
12. I.M.	9.	
13. A.S.	½.	
14. R.H.	2.	
15. E.McG	5.	5.
16. I.K.	1½.	4.
17. M.McM	9.	
18. M.A.	8.	
19. M.A.	9.	
20. R.A.	7.	3.
21. J.L.	9.	
22. S.S.	36.	
23. M.W.	6.	
24. A.Y.	7½.	
25. M.McA	3.	

TABLE 5a.

Group.	No. of patients and duration of their history till induction of pneumothorax.					Percentage with history under 1 yr.
	0 - 3/12	3 - 6/12	6 - 9/12	9 - 12/12	over one yr.	
X	2	5	6	6	6	76
Y	1	8	5	7	4	84
Z	8	4	8	3	2	92

TABLE 5b.

Group.	No. of patients and duration of their history from ipsilateral pleurisy till induction of pneumothorax					Percentage with history under 1 yr.
	0 - 3/12	3 - 6/12	6 - 9/12	9 - 12/12	over one yr.	
X	2	2	3	1	2	80
Y	6	4	2	1	1	92
Z	4	3	1	0	0	100

It is evident from Tables 5a and 5b that the duration of the patient's history, either from the onset of symptoms or from the occurrence of an ipsilateral pleurisy, shows a marked tendency to be shorter in the effusion groups than in the dry group.

TABLE 6.

THE INCIDENCE OF PLEURAL ADHESIONS AND THEIR COMPLEXITY.

Group.	Adhesions.			Cuttable or (?) cuttable.	Uncuttable.	None to cut.
	None.	Few.	Many.			
X.	7%.	24%.	69%.	41%.	52%.	7%.
Y.	0%.	32%.	68%.	40%.	60%.	0%.
Z.	4%.	16%.	80%.	28%.	68%.	4%.

Table 6 was compiled on the basis of thoracoscopic findings, where available, supplemented by the examination of skiagrams. The results indicate that a high percentage of all the pneumothoraces under consideration were complicated by adhesions and that in a majority of pneumothoraces in each group many adhesions were present. Also, in those patients who developed a pleural effusion, the adhesions present were uncuttable in a higher percentage than in Group X whose patients remained free of fluid. It may be deduced from these results that although the presence of adhesions, especially of the more complex types, bears a relation to the incidence of effusions, some knowledge of their pathology and of that of the lung adjacent to them is essential in order to explain the high incidence of adhesions in the patients whose pleural cavities remained dry. This can best be attained/

attained in the living subject by means of the thoracoscope. An analysis of the findings obtained by such an examination will therefore next be presented. It is unfortunate that many patients did not have a thoracoscopy performed, but the findings available may shed some light on the problem.

TABLE 7. SUMMARY OF THORACOSCOPIC FINDINGS.

Group.	No.	Tubercles present.		Lung-containing adhesions.		Strings and cords.		Bands and curtains.		Number cut.
		No.	%.	No.	%.	No.	%.	No.	%.	
X.	13.	4.	30.	5.	38.	3.	23.	10.	77.	8.
Y.	11.	4.	36.	5.	45.	3.	27.	8.	73.	8.
Z.	12.	5.	41.	9.	75.	3.	25.	9.	75.	7.

(Percentage results are given to the nearest whole number).

The figures and percentages given in the preceding table are based on such a small number of thoracoscopic examinations in each group, that they cannot have any great significance. However, the general trend of the findings may be noted. Evidence of subpleural involvement of the lung as shown by the presence of visible tubercles is more frequent in/

in the effusion Groups Y and Z. These tubercles are, in all probability, of recent origin for had they appeared before the induction of a pneumothorax, pleural adhesions would have formed. The percentage of the larger and more complex adhesions is much the same in all groups, but in Group Z, the incidence of lung-containing adhesions is much greater than in either of the other groups. Thus it would appear that the presence of recent sub-pleural lesions may have some influence on the occurrence of effusions and so also may the presence of lung in the pleural adhesions. The lung tissue extending into such adhesions will often be the seat of tuberculous disease and therefore a potential source of tubercle bacilli. In addition, tubercle bacilli may be liberated from the lymphatic spaces present in adhesions of recent origin, if these be punctured.

A short summary of the findings derived from Tables 4 to 7 is now appended.

(1) The shorter the duration of the patient's history of active disease in the lung parenchyma or pleural cavity, the more frequent is the occurrence of a pleural effusion once a pneumothorax is induced.

(2) The more numerous and complex are the adhesions in/

in a pneumothorax, the more often will an effusion occur.

(3) Effusions are commoner in patients showing evidence of recent subpleural involvement.

One does not find much information in the literature to confirm the first observation as relevant statistics are lacking. However, many authors are agreed that the more numerous and complex are the adhesions present in a pneumothorax, the more frequent will be the complication of fluid formation. Among such workers may be mentioned Davies (11), Goorwitch (20) and Simmonds (21). The latter states that "effusion is almost twice as common when adhesions cannot be completely freed as when a free pleura is obtained." Concerning the observation that recent subpleural involvement of the lung is associated with fluid formation in a pneumothorax, the writer finds that various workers are in complete agreement with this finding. In fact, Packard, Hayes and Blanchet (1), state "it would seem that the most common pathogenesis of pleural exudate in man is the direct extension of an active sub-pleural focus through the allergic visceral pleura. By the aid of the thoracoscope subpleural/

subpleural tubercles are frequently seen and occasionally patches of exudate on the pleura have been observed." Peters and Wooley (18) remark that "the conception of an endogenous re-infection of, or migration of bacilli to, the pleura is in accordance with the observed facts." Burrell (22) is very emphatic in his statement that a tuberculous pleurisy is the cause of such effusions, and he notes that only once in artificial pneumothorax used for diseases other than pulmonary tuberculosis has he found an effusion, this being in a patient with a lung abscess.

As pleural adhesions and sub-pleural tubercles seem to bear a definite relation to the occurrence of a pleural effusion, it should be illuminating to consider next the time of onset of effusions after the commencement of pneumothorax therapy. The induction of a pneumothorax is the creation of a space between two endothelial layers which, in their natural circumstances, would tend to react to the presence of superficial parenchymatous tuberculous lesions by localised pleurisy which is, in fact, the origin of the adhesions already discussed. Unfortunately/

Unfortunately, the space created by the operator is uncontrollable. It is quite widely recognised that the degree of lung collapse attained following the first introduction of air, is often greater than could be accounted for by the amount of air introduced from the pneumothorax apparatus. This being so, it might be expected that the spread of tuberculous infection to the pleural cavity would be most likely to occur in the earlier months of treatment. Adhesions are being stretched at this time and caseating tubercles may easily rupture into the pleural cavity, no adhesion formation being possible to prevent this complication.

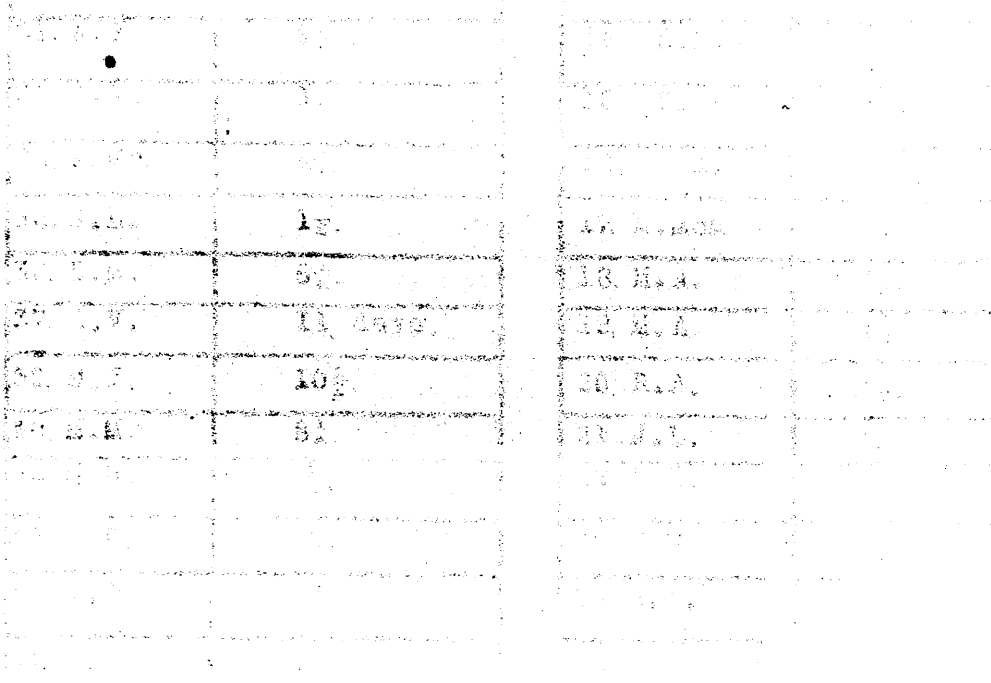


TABLE 9a

TIME ELAPSING BETWEEN INDUCTION OF PNEUMOTHORAX AND DEVELOPMENT OF AN EFFUSION.

Group Y.

No. and Initials.	Period in months.
3. M.F.	16¼.
4. A.McN	6¾.
5. C.H.	1.
6. M.J.	6¼.
7. A.McI.	1¼.
9. M.B.	1¼.
10. M.Mc.A.	1¾.
13. G.McC.	14¾.
14. E.S.	7¼.
15. E.W.	2¾.
22. A.L.	2¼.
23. M.B.	2.
29. J.W.	3¼.
31. A.F.	9½.
32. A.K.	1.
34. A.McN	4½.
35. J.L.	1½.
36. D.M.	6¼.
37. A.V.	11 days.
39. M.F.	10½.
40. M.M.	8¼.
42. M.W.	½.
43. J.B.	¾.
44. M.T.	5.
47. J.B.	1¾.

Group Z.

No. and Initials.	Period in months.
1. A.L.	8¾.
2. M.B.	2¼.
3. S.I.	2¾.
4. C.C.	2.
5. R.L.	3.
6. A.R.	13.
7. C.McK.	2.
8. J.H.	3.
9. H.McG.	2.
10. M.W.	1.
11. A.H.	2.
12. I.M.	12.
13. A.S.	2.
14. R.H.	1½.
15. E.McC	9½.
16. I.K.	2.
17. M.McM	4.
18. M.A.	4¾.
19. M.A.	1½.
20. R.A.	1½.
21. J.L.	5.
22. S.S.	6.
23. M.W.	6½.
24. A.Y.	1.
25. M.McA.	6.

TABLE 9b

	Group Y.	Group Z
No. of patients developing an effusion in the first 3 months	13	15
No.of patients developing an effusion in the first 6 months	16	20
No.of patients developing an effusion in the first 9 months	21	22
No.of patients developing an effusion in the first year	23	24
No. of patients developing an effusion in the first 15 months	24	25
No. of patients developing an effusion in the first 18 months	25	
Total number of patients	25	25

It is evident from Table 9b that most effusions did occur in the earlier months of treatment. By the end of six months of pneumothorax treatment 64% of the patients in Group Y and 80% of the patients in Group Z had their course of treatment complicated by a pleural effusions, and by the end of twelve months, 92% of Group Y patients and 96% of Group Z patients were similarly embarrassed. Peters and Wooley (18) give very similar figures, offering 76% within 6 months and 95% within twelve months, their total number of patients with effusion being seventy-nine.

Packard/

Packard, Hayes and Blanchet (1) give somewhat lower percentages in their series - 58% within six months, and 73% within twelve months.

Having observed then that pleurisy with effusion is definitely related to the earlier months of pneumothorax treatment in a majority of patients, a time at which the tuberculous lesions, pulmonary or pleural, are still in an active state, it is opportune now to proceed to consider in more detail the mechanism of the production of an effusion. There is a considerable difference of opinion among various authors as to what is the immediate precipitating factor in the causation of a pleural effusion. Bard (23) is convinced that practically all severe pleurisies are due to pleuro-pulmonary perforations, but Dumarest, quoted by Packard, Hayes and Blanchet (1), found no evidence of bronchopleural fistulae on observing the manometric pressures in patients developing pleural effusions during pneumothorax treatment. Bard (23) used the Béclère technique to demonstrate his contention. This consists in taking a manometric reading in a suspected spontaneous pneumothorax, connecting the tubing next to a bottle of/

of water and making the patient cough, watching for bubbles to appear and then taking another reading. The pressures will now have fallen. If the patient is then allowed to breathe quietly the original pressure reading will be regained in one to two minutes.

Ford (24), believes that all pleural effusions complicating pneumothorax are due to the breaking down of adhesions. Gloyne (25) considers that if an adhesion be ruptured at a point at which tubercle bacilli can be liberated into the pleural sac, a secondary effusion is likely to follow. This, he states, is probably what happens from time to time in cases of pleural effusion complicating artificial pneumothorax. Wollaston (26) thinks that the stress imposed on a diseased area of lung by the presence of adhesions is of such importance in the causation of a pleural effusion that he is prepared to perform thoracoscopy and adhesion section, if the latter be possible, even in the presence of an acute effusion. Of five such patients on whom he operated, in three the temperature fell after the adhesion section and the effusion, which was aspirated, did not recur. In 1936, Korol (27), in an article on "Haemorrhagic Pleurisy of Tuberculous Origin and

Haemopneumothorax," stated that "the widespread use of artificial pneumothorax in the treatment of pulmonary tuberculosis has brought about an increased incidence of haemorrhagic pleurisy, the majority of cases in the past fifteen years having been reported in connection with artificial pneumothorax. In all there are records of thirty cases." He believes that bleeding from the stump of a torn adhesion is the cause of such effusions. He notes, however, that a progressive ulcerating tuberculous lesion in the lung parenchyma may extend to a point at which it may involve the visceral pleura and a large blood vessel. Such a happening is rare. It is apparently not so uncommon for a caseating sub-pleural focus to extend into the pleural cavity during artificial pneumothorax therapy. Matson, Matson and Bisaillon (28), infer from a study of empyema occurring during pneumothorax therapy that a sub-pleural tuberculous lesion is of more importance in producing an empyema than is the tearing of lung cortex, for adhesions were absent in fifty per cent. of their empyema cases. Goorwitch (20), is of a similar opinion stating that "the clinical manifestations of a pleural effusion occurring during pneumothorax therapy probably depend to/

to a high degree on the quantity of caseous tissue and tubercle bacilli spilled from superficial ulcerative pulmonary lesions into the pleural sac." Simmonds (21), remarking that at Clare Hall Sanatorium pleural effusion was seven times as frequent in patients treated by artificial pneumothorax than in those not so treated, suggests that this is due to the opening of the lung spaces, especially pulmonary cavities, into the pleural cavity. Hutchinson and Blair (29) also believe that an effusion occurring during artifical pneumothorax induced for pulmonary tuberculosis is often the result of a small rupture of the lung, supporting their opinion by the fact that an effusion is often preceded by a rise of intrapleural pressure and that the temperature which accompanies its development is very similar to that seen in ordinary cases of spontaneous pneumothorax.

From the preceding review of the literature of this aspect of the subject, it appears that there is a general consensus of opinion that an effusion is preceded by some change at the surface of the lung. This may be the spilling of tuberculous material into the pleural cavity with or without a frank lung rupture/

rupture. The clinical findings in the writer's series should assist in elucidating the problem. No mention will be made at present of the haematological findings as they can most suitably be studied in a separate section.

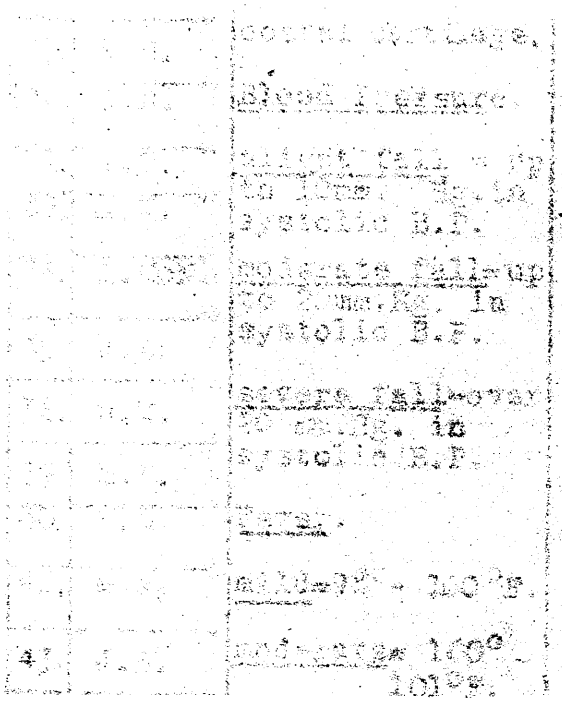


Table 10. Group Y.

No.	Initials.	Malaise.	Loss of Appetite.	Vomiting.	Dyspnoea.	Pain.	Cough.	Sputum.	Weight.	Fever. Degree.	Duration (in days).	Blood Pressure.	Amount of Effusion.
3.	M.P..	+	+	none.	+	none.	incrd.	incrd.	sl.fall	out-patient.		Sl.fall.	moderate.
4.	A. McN.	+	+	none.	+	+	no change.	no change.	no note.	moderate.	3.	Sl.fall.	moderate.
5.	C.H.	+	+	none.	slight.	none.	no change.	no change.	fell.	mod.-mild.	10.	no fall.	moderate.
6.	M.J.	+	+	+	+	+	incrd.	incrd.	in bed	severe-mod.	26.	no fall.	large.
7.	A.McI.	+	+	none.	+	+	incrd.	no change.	fell.	severe-mod.	9.	no fall.	large.
9.	M.B.	+	+	none.	+	+	no change.	no change.	in bed	severe-mod.	6.	no fall.	moderate.
10.	M.McA.	+	+	none.	+	+	incrd.	incrd.	fell.	severe-mod.	37.	mod.fall.	large.
13.	G.McC.	+	none.	none.	none.	sl.	incrd.	incrd.	+1 lb.	none		no fall.	small.
14.	E.S.	+	+	none.	+	+	incrd.	no change.	fell.	severe-mild.	25.	no fall.	large.
15.	E.W.	+	+	none.	+	+	no change.	no change.	no change.	mod-mild.	5.	mod.fall	large.
22.	A.L.	none.	+	none.	none.	none.	no change.	no change.	Sl.fall	severe-mod.	15.	no fall.	small.
23.	M.B.	+	+	+	+	+	incrd.	incrd.	fell.	mod-mild.	5.	sl.fall.	large.
29.	J.W.	+	+	None.	none.	+	no change.	no change.	in bed	mod.-mild.	2.	no change.	large.
31.	A.F.	+	+	+	+	+	incrd.	incrd.	in bed	severe-mod.	18.	mod.fall.	large.
32.	A.K.	none.	none.	none.	none.	sl.	no change.	no change.	+ 4 lb	moderate.	13.	mod.fall.	small.
34.	A.McN.	+	+	+	+	+	no change.	no change.	no change.	mod-mild.	16.	mod.fall.	large.
35.	J.L.	+	+	none.	+	none.	incrd.	incrd.	in bed	severe-mod.	67.	sl. fall.	moderate
36.	D.M.	+	+	none.	+	+	incrd.	incrd.	in bed	severe-mod.	21.	severe.	large.
39.	M.F.	+	+	none.	+	none.	incrd.	incrd.	in bed	none.		no fall.	large.
40.	M.M.	none.	none.	none.	none.	none.	no change.	no change.	in bed	mild.	5.	no fall.	moderate.
42.	M.W.	none.	none.	none.	none.	none.	no change.	no change.	fell.	Mod-mild.	14.	no fall.	moderate.
43.	J.B.	+	+	none.	++	+	incrd.	incrd.	fell.	mild.	23.	no fall.	large.
44.	M.T.	+	+	none.	none.	+	no change.	no change.	fell.	mild.	1.	no fall.	large.
45.	M.R.	+	+	+	none.	none.	no change.	no change.	fell	unknown.		no note.	moderate.
47.	J.B.	+	+	none.	+	none.	incrd.	incrd.	no change	mild.	2.	severe fall.	large.

Explanatory Note

incrd.=increased.

sl. = slight.

mod.= moderate.

Effusion.

Small = up to 3 fingerbreadths or 6th costal cartilage.

moderate=up to 5 fingerbreadths or 5th costal cartilage.

large = over 5 fingerbreadths or above 5th costal cartilage.

Blood Pressure.

slight fall = up to 10mm. Hg.in systolic B.P.

moderate fall=up to 20mm.Hg. in systolic B.P.

severe fall-over 20 mm.Hg. in systolic B.P.

Fever.

mild=98°- 100°F.

moderate= 100° - 101°F.

severe=over 101°F.

Table 10. Group Z.

No.	Initials.	Malaise.	Loss of Appetite.	Vomiting	Dyspnoea.	Pain.	Cough.	Sputum	Weight	Fever Degree.	Fever Duration. (in days)	Amount of effusion.
1.	A.L.	+	+	none.	slight.	none.	no change.	no change.	no change.	mild.	9.	large.
2.	M.B.	No notes available.....							no change.	moderate.	10.	large.
3.	S.I.	+	+	none.	slight.	+	no change.	no change.	fell.	mod.-severe.	25.	moderate.
4.	C.C.	+	+	+	slight.	none.	no change.	no change.	fell.	mild-mod.	6.	small.
5.	R.L.	+	+	none.	+	none.	incrd.	incrd.	fell.	mod.-severe.	35.	moderate.
6.	A.R.	+	+	none.	+	sl.	no change.	no change.	+ 21b.	mild.	7.	moderate.
7.	C.McK.	+	+	+	+	sl.	no change.	no change.	in bed	mild.	19.	moderate.
8.	J.H.	none.	none.	none.	none.	none.	no change.	no change.	in bed	mild.	3.	moderate.
9.	H.McG.	+	+	none.	+	+	incrd.	incrd.	in bed	mild-mod.	18.	moderate.
10.	M.W.	+	+	+	+	+	no change.	no change.	fell.	mild.	16.	moderate.
11.	A.H.	none.	none.	none.	none.	none.	no change.	no change.	in bed	moderate.	4.	moderate.
12.	I.M.	none.	none.	none.	none.	none.	no change.	no change.	no change	none.		small.
13.	A.S.	none.	none.	none.	none.	none.	no change.	no change.	in bed	mild.	4.	moderate.
14.	R.H.	none.	none.	none.	none.	none.	no change.	no change.	+ 7lb.	mild.	2.	moderate.
15.	E.McC.	+	+	none.	+	none.	incrd.	incrd.	fell.	moderate.	21.	moderate.
16.	I.K.	+	+	+	+	+	incrd.	incrd.	fell.	mod.-severe.	24.	large.
17.	M.McM.	+	+	none.	slight.	+	no change.	no change.	fell.	mild-mod.	8.	moderate.
18.	M.A.	none.	none.	None.	None.	None.	no change.	no change.	fell.	none.		moderate.
19.	M.A.	none.	none.	none.	none.	none.	no change.	no change.	fell.	mild-mod.	19.	moderate.
20.	R.A.	None.	none.	none.	slight.	none.	no change.	no change.	fell.	out-patient.		moderate.
21.	J.L.	+	+	none.	none.	+	no change.	no change.	- 3lb.	mild.	7.	moderate.
22.	S.S.	+	+	none.	slight.	none.	incrd.	incrd.	fell.	mild.	5.	moderate.
23.	M.W.	+	+	+	+	+	incrd.	incrd.	fell.	mild.	5.	moderate.
24.	A.Y.	+	+	none.	+	none.	incrd.	no change.	in bed.	moderate.	28.	large.
25.	M.McA.	none.	none.	none.	none.	none.	no change.	no change.	fell.	confinement at another Hosp.		large.

Explanatory Note.

incrd.= increased.

sl. = slight.

mod.= moderate.

Effusion.

Small-up to 3 fingerbreadths or 6th costal cartilage

moderate = up to 5 fingerbreadths or 5th costal cartilage.

large = over 5 fingerbreadths or above 5th costal cartilage.

Fever

Mild = 98° - 100° F.

Moderate=100° - 101° F.

Severe= over 101° F.

TABLE 11.

	Group Y.	Group Z.
Systemic upset.	88%.	60%.
Dyspnoea.	64%.	60%.
Pain.	64%.	36%.
Increased Cough.	48%.	24%.
Increased sputum.	44%.	24%.
Fall in weight.	44%.	36%.
Fever.	84%.	84%.
Fall in blood pressure.	44%.	no note.

An analysis of the findings presented leads to several conclusions:-

(1) In a high percentage of patients a systemic upset coincides with the onset of a pleural effusion. This upset is generally accompanied by fever of varying degree, and a fall in blood pressure and in weight may also occur. The latter generally appear when the systemic disturbance and fever are most severe but this is not invariable. They are reflections of an exacerbation of the tuberculous process.

(2) Dyspnoea is present in a considerable proportion of patients (60 - 64%). This lends support to the theory that in many of these patients a spontaneous pneumothorax occurs before the onset of an effusion.

(3)/

(3) Increased cough and sputum, although not noted as occurring so frequently as dyspnoea, are nevertheless increased in quite a number of patients (24 - 48%). These are more difficult for the patient to assess than is dyspnoea, and individual daily records are not kept in this hospital of the amount of sputum expectorated in each twenty-four hours. This is due to the shortage of suitable measuring flasks. Thus, these findings may also be taken to lend support to the spontaneous pneumothorax theory mentioned previously as being of importance in the production of a pleural effusion.

(4) Pain in the chest was frequent in one group of patients, occurring in 64%, but in the other group it was noted in only 36% of patients. This indicates that there is, in many patients, an acute inflammation of the pleura at the commencement of an effusion. That such inflammation does occur is confirmed by the fever and systemic upset previously observed. In addition, it is noted quite frequently in this hospital, that patients who are developing a pleural effusion complain of more severe pain on puncturing the pleura than they have formerly experienced. This was very marked

in/

in one patient in the present series, (Group Y, 36, D.M).

Before discussing this subject farther, it may be profitable to consider the mean intrapleural pressures noted before, during and after the onset of an effusion.

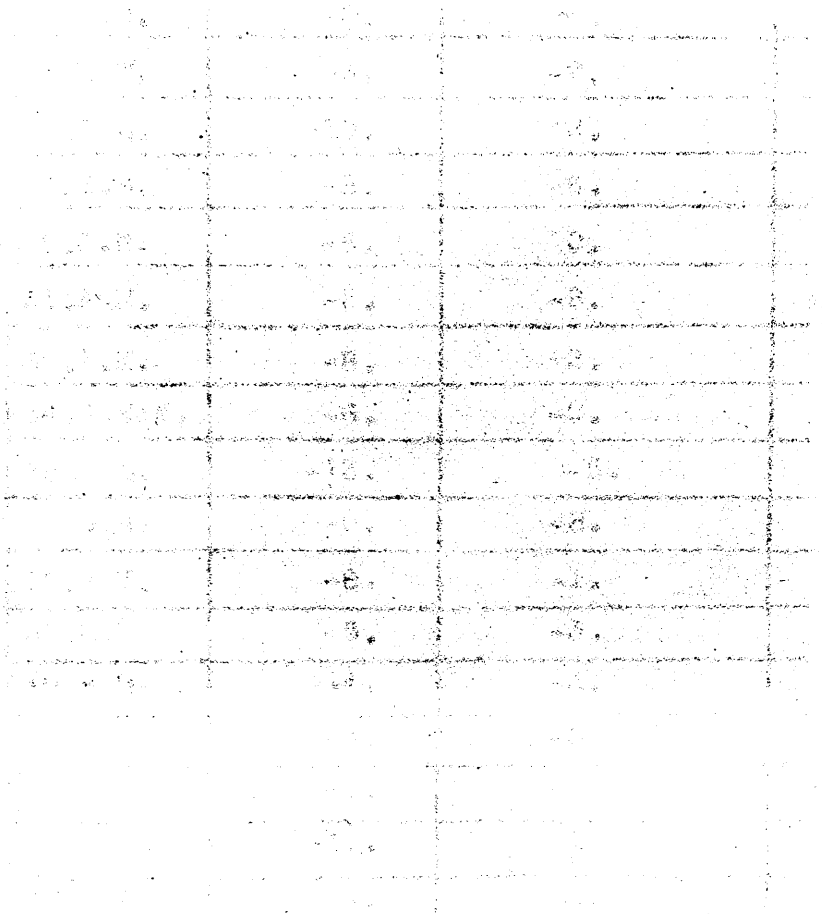


Table 12.

ANALYSIS OF INTRAPLEURAL PRESSURE. GROUP Y.

No. and Initials.	Average mean pressure readings.		
	Pleura dry.	Coincident with effusion.	After onset of effusion.
3. M.P.	-2.	unknown.	-8.
4. A.McN.	-12.	-7.	-2.
5. C.H.	-11.	-11.	+6.
6.M.J.	-5.	-3.	no reading.
7. A.McI.	-8.	-8.	-1.
9. M.B.	-7.	-3.	-2.
10.M.McA.	-6.	-2.	-2.
13.G.McC.	-10.	-6.	no reading.
14.E.S.	-5.	+4.	0.
15.E.W.	-6.	-2.	-2.
22.A.L.	-10.	+2.	+3.
23.M.B.	-8.	-6.	0.
29.J.W.	-6.	0.	+2.
31.A.F.	-5.	-8.	no reading.
32.A.K.	-8.	+2.	+1.
34.A.McN.	-6.	-2.	-3.
35.J.L.	-13.	-5.	+1.
36.D.M.	-9.	-8.	no reading.
37.A.V.	-8.	-1.	-2.
39.M.F.	-5.	-3.	-3.
40.M.M.	-4.	-3.	0.
42.M.W.	-5.	-6.	+5.
43.J.B.	-6.	-7.	-2.
44.M.T.	-13.	-1.	no reading.
47.J.B.	-4.	-2.	-1.

(Each rise or fall of two divisions on water manometer equals one centimetre.)

Table 12.

ANALYSIS OF INTRAPLEURAL PRESSURE. GROUP Z.

No. and Initials.	Average mean pressure readings.		
	Pleura dry.	Coincident with effusion.	After onset of effusion.
1. A.L.	-8.	-1.	no reading.
2. M.B.	-6.	-2.	+5.
3. S.I.	-7.	+1.	+3.
4. C.C.	-4.	-5.	+20.
5. R.L.	-6.	-2.	-4.
6. A.R.	-8.	+6.	-4.
7. C.McK.	-8.	-6.	-2.
8. J.H.	-8.	-3.	-2.
9. H.McG.	unknown.	unknown.	-1.
10.M.W.	-11.	-5.	-4.
11.A.H.	-4.	-4.	-3.
12.I.M.	-9.	-4.	-2.
13.A.S.	-9.	+1.	+2.
14.R.H.	-11.	-8.	-14.
15.E.McC.	-6.	-4.	+5.
16.I.K.	-4.	0.	+2.
17.M.McM.	-9.	-9.	-4.
18.M.A.	-7.	unknown.	-2.
19.M.A.	-8.	-2.	+1.
20.R.A.	unknown.	unknown.	-3.
21.J.L.	-12.	-8.	died.
22.S.S.	-16.	-10.	no reading.
23.M.W.	-5.	-2.	no reading.
24.A.Y.	-8.	-6.	no reading.
25.M.McA.	-7.	unknown.	+1.

TABLE 13.
SUMMARY OF INTRAPLEURAL PRESSURE FINDINGS.

	Group Y.		Group Z.	
	No.	%.	No.	%.
During evolution of effusion				
1. Rise in pressure.	19.	76.	18.	72.
2. No change in pressure.	2.	8.	2.	8.
3. Fall in pressure.	3.	12.	1.	4.
4. Pressure unknown.	1.	4.	4.	16.
After onset of effusion.				
1. Farther rise in pressure.	12.	48.	13.	52.
2. No change in pressure.	3.	12.	1.	4.
3. Fall in pressure.	4.	16.	3.	12.
4. Pressure unknown.	6.	24.	8.	32.

Note:- The average mean pressure in the preceding tables was calculated by averaging the mean pressure before and after a refill on two occasions during the appropriate periods referred to.

Considering the clinical findings as summarised in the two previous tables, it is obvious that in a majority of patients the onset of a pleural effusion during artificial pneumothorax therapy is accompanied by a syndrome such as might be produced by the exacerbation of tuberculous disease within the pleural cavity. The increase in intrapleural pressure is strongly suggestive of the addition of air to the pneumothorax/

pneumothorax. This air, as previously explained, can have been added only by the rupture of lung tissue. This may have taken place by the perforation of a cavity or the ulceration of a subpleural caseous focus with or without the drag of an adhesion on the area rupturing. Bard (23) has demonstrated that such lung ruptures are often valvular. That no change in intrapleural pressure was recorded in 8% of patients in both groups Y and Z can be explained by the fact that tubercle bacilli may be liberated from a caseous area or from the rupture of recent adhesions, which, as Gloyne (25) has shown, may harbour tubercle bacilli, without any leak of air occurring from the lung itself. The writer suggests that the fall in intrapleural pressure which occurred in three patients of Group Y and one patient of group Z may have been due to the increased permeability of an acutely inflamed pleura leading to an increased absorption of air, no spontaneous pneumothorax having occurred in these patients. Pinner, Moerke and Saley (5) state that inflammation increases the permeability of capillaries and endothelial linings and that this mechanism must be assumed for the pleura. Up to this point, quoted authority and the writer's investigations show that whatever the change in the pleural cavity, it has its origin in the almost unnatural/

unnatural separation of the pleural layers whereby stresses are put on adhesions, support is taken away from lung cavities, and subpleural tubercles which, in nature, might have resulted in further adhesions, find themselves literally out of touch with the parietal pleura. From any of these sources the shedding of tubercle bacilli on to the allergic pleural surfaces will be ample enough cause for the development of an effusion. It follows that the finding of tubercle bacilli in the now developed fluid should be an almost constant occurrence and with the questions raised by these thoughts the following paragraphs are intended to deal. For the sake of completeness reference is made to the cytological examination of the fluid in a number of patients.

A combination of three methods was used in the search for the tubercle bacillus.

(1) Examination of smears made from the sediment of each effusion. A smear prepared by the antiformin concentration method was examined if the direct smear was negative.

(2) Culture of the sediment on Lowenstein's medium. Four of these specimens became contaminated by moulds.

(3) Guinea-pig inoculation, when necessary.

TABLE 14. GROUP Y.

No. and Initials.	Direct smear.	Antiformin concentratn. method.	Lowenstein culture.	Guinea-pig inoculation	No. of exams.
3. M.P.	Neg.	Neg.	Neg.	Neg.	2.
4. A.McN.	Pos.(1).	Pos.(1).	Pos.(4).	Pos.(1). Neg.(1).	4.
5. C.H.	Neg.	Neg.	Neg.	Pos.(1). Neg.(1).	3.
6. M.J.	Pos.(1).	Not done	Pos.(1).	Not done.	1.
7. A.McI.	Pos.(1).	Neg.	Neg.	Pos.(1).	2.
9. M.B.	Neg.	Neg.	Neg.	Pos.(1).	1.
10. M.McA	Pos.(1).	Not done	Pos.(1).	Not done.	4.
13. G.McC	Neg.	Neg.	Neg.	Neg.	1.
14. E.S	Neg.	Pos.(1).	Pos.(1).	Neg(1).	3.
15. E.W.	Pos.(9).	Pos.(2).	Pos.(8).	Not done.	11.
22. A.L.	Pos.(1).	Not done	Pos.(1).	Not done.	1.
23. M.B.	Pos.(12.	Pos.(4).	Pos.(17).	Pos.(1).	19.
29. J.W.	Pos.(5).	Not done	Pos.(5).	Pos.(1).	5.
31. A.F.	Pos.(4).	Not done	Pos.(3).C1.	Not done.	4.
32. A.K.	Pos.(2).	Not done	Pos.(2).	Not done.	2.
34. A.McN.	Pos.(5).	Not done	Pos.(5).C1.	Pos(1).	6.
35. J.L.	Pos.(1).	Not done	Pos.(1).	Not done.	1.
36. D.M.	Pos.(2).	Not done	Pos(2).	Not done.	2.
39. M.F.	Pos(2).	Not done	Pos.(1).C1.	Not done.	2.
40. M.M.	Pos.(3).	Not done	Pos.(3).	Not done.	3.
42. M.W.	Pos.(5).	Not done	Pos.(5).	Not done.	5.
43. J.B.	Pos.(9).	Not done	Pos.(9).	Neg.(1).	10.
44. M.T.	Pos.(1).	Neg.(2).	Pos.(3).	Not done.	3.
45. M.R.	Pos.(1).	Not done	Pos.(1).	Not done.	1.
47. J.B.	Pos.(3).	Neg.(2).	Pos.(2).C1.	Pos.(1).	5.

C1. - Contaminated once.

TABLE 14. GROUP Z.

No. and Initials.	Direct smear.	Antiformin concentration method.	Lowenstein culture.	Guinea-pig inoculation.	No. of exams.
1. A.L.	Neg.	Neg.	Pos.	Pos.	1.
2. M.B.	Pos.	Not done.	Pos.	Not done.	1.
3. S.I.	Pos.	Not done.	Pos.	Not done.	1.
4. C.C.	Pos.	Not done.	Pos.	Not done.	1.
5. R.L.	Pos.	Not done.	Pos.	Not done.	1.
6. A.R.	Neg.	Pos.	Pos.	Not done.	1.
7. C.McK.	Pos.	Not done.	Pos.	Not done.	1.
8. J.H.	Pos.	Not done.	Pos.	Not done.	1.
9. H.McG.	Pos.(1).	Neg.(1).	Pos.(1).	Not done.	2.
10. M.W.	Neg.	Neg.	Neg.	Pos.	1.
11. A.H.	Neg.	Neg.	Pos.	Pos.	1.
12. I.M.	Pos.	Not done.	Pos.	Not done.	1.
13. A.S.	Pos.	Not done.	Pos.	Not done.	1.
14. R.H.	Pos.	Neg.	Neg.	Pos.	1.
15. E.McC	Pos.	Not done.	Pos.	Not done.	1.
16. I.K.	Pos.	Not done.	Pos.	Not done.	1.
17. M.McM	Pos.	Not done.	Pos.	Not done.	1.
18. M.A.	Pos.	Not done.	Pos.	Not done.	1.
19. M.A.	Neg.	Neg.	Pos.	Pos.	1.
20. R.A.	Neg.	Neg.	Pos.	Pos.	1.
21. J.L.	Neg.	Neg.	Neg.	Neg.	1.
22. S.S.	Pos.	Not done.	Pos.	Not done.	1.
23. M.W.	Pos.	Not done.	Pos.	Not done.	1.
24. A.Y.	Neg.	Neg.	Neg.	Neg.	1.
25. M.McA.	Neg.(2).	Pos.(1).	Pos.(1).	Pos.(1).	2.

Table 14a. SUMMARY OF TABLE 14.

Group Y. Total of 25 patients.

Result.	Direct smear.	Antiformin concentratn method.	Lowenstein culture.	Guinea-pig inoculation.
Positive.	20.	4.	20.	8.
Negative.	5.	8.	5.	5.
Not done.	0.	13.	0.	12.
Percentage Positive.	80% of 25.	33% of 12.	80% of 25.	61% of 13.
Percentage positive combining all methods = 92%				

Group Z. Total of 25 patients.

Result.	Direct smear.	Antiformin concentratn method.	Lowenstein culture.	Guinea-pig inoculation.
Positive.	16.	2.	21.	7.
Negative.	9.	9.	4.	2.
Not done.	0.	14.	0.	16.
Percentage Positive.	64% of 25.	18% of 11.	84% of 25.	77% of 9.
Percentage positive combining all methods = 92%				

Table 15.

	Group Y.		Group Z.	
	No.	%.	No.	%.
Patients positive by concentration method when direct smear was negative.	1.	4.	2.	8.
Patients positive by Lowenstein culture when all smears were negative.	0.	0.	4.	16.
Patients positive by guinea-pig inoculation when all other methods were negative.	2.	8.	1.	4.

From the preceding tables, conclusive proof of the infection of the pleural cavity by tubercle bacilli is demonstrated in a very high percentage (92%), of the fifty patients who had an effusion. Direct smear examination reveals tubercle bacilli in an average of 72% of patients and this figure is further increased to 76% when examination of smears prepared by the antiformin concentration method is included. Lowenstein's medium used for culturing tubercle bacilli, provided further aid in their detection in these effusions, for the average figure of positive findings rises to 84% when the cultural method is included. Guinea-pig inoculation finally increases the average percentage of positive results to 92%.

In view of these findings, it is rather surprising to find Ustvedt (30), stating in his handbook of pulmonary tuberculosis published in 1942 that "the cause of effusions occurring in artificial pneumothorax is not yet established." He remarks that "presumably in most cases the tuberculous process spreads to the pleura and involves its surface." On the other hand we find Wingfield (31), observing that "these effusions are always sterile but usually contain tubercle bacilli. These are more common in the purulent effusions, but could/

could probably be found in every case if a sufficiently careful search were made." Burrell (32) believes that the direct cause of effusion in pneumothorax treatment, as in ordinary cases of pleural effusion, is infection by the tubercle bacillus. He gives reasons for this belief, but no figures reporting the number of times tubercle bacilli were found, stating only that "they are almost always present in a long standing case." Davies(11) points out that tubercle bacilli are often very difficult to demonstrate in serous effusions unless guinea-pig inoculation be used, and Peters and Wooley (18), in their series, were able to demonstrate tubercle bacilli by direct smear examination in only four out of thirty-seven cases of pleural effusion. By guinea-pig inoculation they were, however, able to confirm the presence of tubercle bacilli in 80% of their specimens. Pinner, Moerke and Saley (5), who found tubercle bacilli in the fluid taken from twelve out of fifteen patients , and Oshima, Suzuki and Suzuki, who demonstrated tubercle bacilli by cultural methods in 90% of twenty pneumothorax effusions, are quoted by Alexander (10), who concludes that "the vast majority of all pneumothorax effusions are true tuberculous pleuritides." Brock, Mullen and Woodson (33) found tubercle bacilli in 100% of twenty-eight effusions complicating/

complicating artificial pneumothorax, and they state that "effusions developing subsequent to the collapse of tuberculous lungs are not only always tuberculous in nature but tubercle bacilli can be found in nearly every case if the proper procedure of examination is followed." The methods they used were direct smear examination, culture and guinea-pig inoculation, the latter being done when direct smears were negative. They give no account of the percentage of positive results achieved by each method. Weisman (15) reporting on twenty-five specimens examined, found only four positive by direct smear examination and six positive by guinea-pig inoculation. Goorwitch (19) reporting on effusions following intrapleural pneumolysis, found tubercle bacilli in 30% of one hundred and twenty-one effusions by direct smear examination and in 77% of ninety-four effusions by the culture method. Rosenthal (34) lays considerable stress on the importance of trauma in the aetiology of effusions in artificial pneumothorax and believes that only a relatively small proportion are due to a tuberculous pleurisy. He gives no figures relating to examinations for the tubercle bacillus nor does

Quisumbing (35), who agrees with Ustvedt in stating that "we are still very much in the dark regarding the matter."

It is thus evident that the writer's bacteriological findings agree substantially with those of several other workers whose opinion may be taken as reliable. It may be added here that in only two patients, each of whom had an empyema, did the writer find any evidence of secondary infection in the fifty patients having effusions in his series. One of these patients had a spontaneous pneumothorax; the pleural cavity of the other was accidentally contaminated during the aspiration of fluid.

Turning next to the cytology of these effusions we find Gloyne (2), stating that "the mild serous effusions have much the same characters as the secondary serous effusions of frank open pulmonary tuberculosis, show a lymphocytic predominance in the cell count with three per cent. of protein or more, and are sterile on culture. As the fluid becomes more opalescent and reaches the sero-purulent stage the polymorphs increase and finally dominate the picture." Gloyne also believes that if there are many polymorphs together with tubercle bacilli, this is strong presumptive/

presumptive evidence of a spontaneous pneumothorax. In the series of patients under consideration the cytology of their pleural effusions was carried out in Group Y only. Difficulty was experienced from time to time in distinguishing cell types. From the following table the cytology of the fluid at the initial aspiration will be given. Contractions used in this next table are as follows:-

N - Neutrophils. E - Eosinophils.

B - Basophils. S.L.- Small Lymphocytes.

L.L- Large Lymphocytes. M - Monocytes.

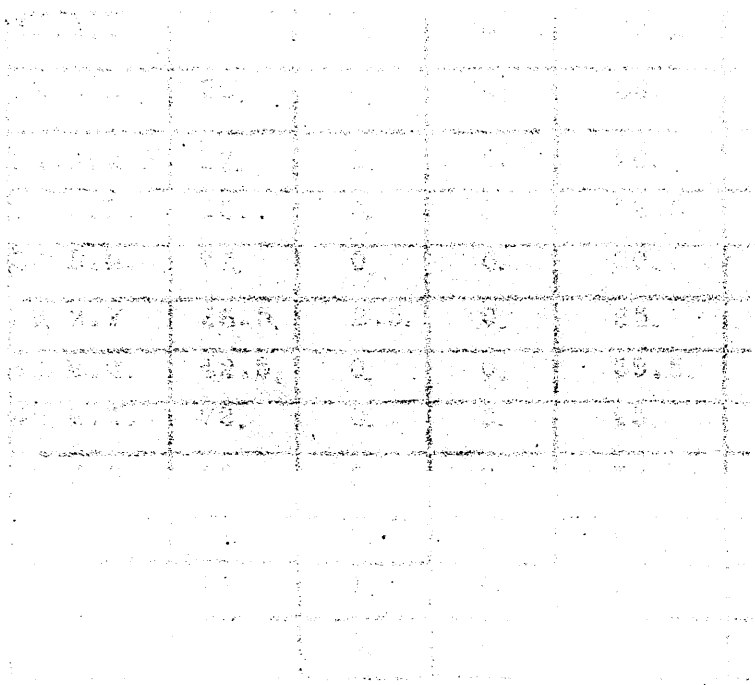


TABLE 16.

CYTOLOGY OF PLEURAL FLUID AT INITIAL ASPIRATION.

No. and Initials	N.	E.	B.	S.L.	L.L.	M.
3. M.P.	2.	3.5.	0.	88.	2.5.	4.
4. A.McN	13.	0.5.	0.	62.	1.5.	23.
5. C.H.	46.	2.5.	0.	48.	2.	1.5.
6. M.J.	20.	0.	0.	74.5.	3.5.	2.
7. A.McI.	45.5.	2.	0.	44.5.	8.	0.
9. M.B.	29.	15.	0.	54.	0.5.	1.5.
10. M.McA.	32.	0.	0.	55.	3.5.	9.5.
13. G.McC.	5.	3.5.	0.	82.	7.5.	2.
14. E.S.	67.	0.5.	0.	26.5.	2.	4.
15. E.W.	48.	0.	0.	17.	0.	35.
22. A.L.	90.	0.	0.	4.5.	0.	5.5.
23. M.B.	8.	1.	0.	74.	5.	12.
29. J.W.	95.	0.	0.	3.5.	1.	0.5.
31. A.F.	18.	0.	0.	79.5.	2.	0.5.
32. A.K.	38.	0.	0.	53.	7.	2.
34. A.McN	17.	1.	0.	70.	8.5.	3.5.
35. J.L.	36.	0.	0.	52.5.	8.	3.5.
36. D.M.	77.	0.	0.	20.	2.5.	0.5.
39. M.F	26.5.	2.5.	0.	65.	2.5.	3.5.
40. M.M.	42.5.	0.	0.	39.5.	11.	7.
42. M.W.	72.	0.	0.	23.	3.	2.
43. J.B.	46.	8.	0.	38.	3.5.	4.5.
44. M.T.	37.	0.	0.	60.5.	2.	0.5.
45. M.R.	77.	1.	0.	9.	9.	4.
47. J.B.	11.	0.	0.	78.	1.5.	0.

From the preceding table it is found that in 76% of the twenty-five patients, their pleural fluid showed a lymphocytic predominance and 24% showed a predominance of polymorphs at the initial examination. Of these patients in whom the polymorphs predominated, all showed tubercle bacilli in direct smear of the centrifuged sediment of the effusion and these were usually present in considerable numbers. Only two of these six patients (Group Y., 14, E.S., 36, D.M), showed evidence suggestive of spontaneous pneumothorax clinically. It may be noted that the cytology in each fluid examined confirms Burrell's (22) contention that these effusions are exudates. It also agrees with Gloyne's (2) description of the cellular types to be found, although those effusions which showed a predominance of polymorphs accompanied by numerous tubercle bacilli, were preceded by clinical signs and symptoms of spontaneous pneumothorax in only thirty-three and one third per cent. of the six cases.

It may be concluded then, that the cytological examinations made by the writer lend further support to his contention that these effusions are essentially tuberculous.

All the Group Y patients except two had a specific gravity estimation done on the specimens of fluid/

fluid obtained. The fluid was insufficient in amount in the two patients excluded. An ordinary urinometer was used and the range of the readings obtained was 1005-1026. All the effusions gave a positive Rivalta's test and the Esbach readings varied between 1.8% and 4% of protein. Thus some of the fluids possessing the characters of exudates also showed the physical characteristics of transudates. Pinner, Moerke and Saley (5), had similar findings in their series of thirty-two specimens. It is the writer's belief that these physico-chemical findings are of little help in elucidating the aetiology of the effusions under consideration, the data obtained being variable and contradictory. The time spent on carrying out these tests could be better employed in more prolonged searching of smears for tubercle bacilli.

Having established the main causative factor in the aetiology of effusion in artificial pneumothorax, we may next consider the predisposing factors stressed in varying degree by different workers.

(1) Trauma.

(a) External trauma. No external trauma was sustained by any patients in the writer's series.

(b) Internal trauma. Internal trauma may take several forms/

forms, such as the use of excessive amounts of air and of positive pressures, the giving of air by inexperienced operators when inadequate manometric oscillations have been recorded, the too rapid introduction of air, the rough introduction of large needles, thoracoscopy and adhesion section.

In this hospital Clive Riviere needles are used for the induction of pneumothorax and for the first refill. Next, an aspiration type of needle, 1.5 mm. in diameter and having a side opening near the point, is used, till the lung is sufficiently collapsed to allow of the use of Kjer-Petersen needles without serious risk of puncturing it. Anaesthesia using 2% Novocaine is employed except when Kjer-Petersen needles are used.

While in hospital, the patients under consideration did not receive amounts of air in excess of four hundred cubic centimetres and generally refills averaged two hundred to three hundred cubic centimetres twice weekly for the first few months of pneumothorax treatment. At the out-patient clinics which a few of the patients had to attend after dismissal from hospital, refills were given less frequently and larger amounts of air, such as five hundred to one thousand cubic centimetres were introduced at intervals of three to six weeks. Only one patient (Group Y, 2, M.P.), developed an/

an effusion while under this regime. She was having refills of four to five hundred cubic centimetres of air at six weekly intervals. It must be recognised that the trauma produced by any given amount of air will vary considerably from patient to patient. Thus one hundred cubic centimetres of air given to a patient with a partially effective pneumothorax complicated by adhesions is much more likely to do harm than five hundred cubic centimetres given into a pneumothorax where the lung is free. Yet, the patient who developed an effusion while receiving large infrequent refills at a clinic, had a pneumothorax in which previous adhesion section while in hospital had completely freed the lung from the chest wall; six other patients with adhesions, which were extensive in two, did not develop an effusion while attending a clinic. It has been the experience of the senior members of the staff of this hospital that it is not wholly unwise to continue refills in patients having uncuttable adhesions. Many of these patients have contralateral disease and the partially effective collapse of the worse lung sometimes permits of a degree of healing which will allow of a thoracoplasty

at/

at a later date. A few patients have in fact had thoracoplasty performed while a contralateral pneumothorax has been maintained, the lung operated upon having previously been partially collapsed by artificial pneumothorax. It is probable that the degree of pleural involvement by active tuberculous disease is more important than is the trauma of large amounts of air. In relation to the use of positive pressures the following tables may be of interest.

TABLE 17a.

Group.	Maximum positive reading. (Swing recorded.)		Most positive average reading.	
	Before refill.	After refill.	Before refill.	After refill.
X.	+18. -14.	+26. -18.	+12.	+8.
Y.	+14. -14.	+18. - 6.	+ 3.	+9.
Z.	+12. - 6.	+18. - 6.	+ 4.	+6.

TABLE 17b.

NO. OF PATIENTS IN EACH GROUP WITH AVERAGE READING ABOVE ZERO.

Group.	Before refill.	After refill.
X.	4.	13.
Y.	2.	10.
Z.	2.	3.

It is seen at a glance that the maximum positive readings were recorded in the non-effusion group and that/

that also this group showed the highest average readings both before and after a refill. In addition, this group had a greater number of patients with average readings above zero, this being more marked after refills. It may therefore be suggested that positive intrapleural pressures per se have not, in this series of patients, been proved to be as important in the aetiology of pleural effusions as many writers suggest. Packard, Hayes and Blanchet (1), and also Peters and Wooley (18) confirm this observation. Davies (11), Rosenthal (34), Leaver and Hardaway (36), Harper (37) and Rao(14), among others, believe that positive intrapleural pressures are of importance in the causation of pleural effusions in artificial pneumothorax. It may be concluded that in certain patients the use of positive intrapleural pressures may predispose to the development of an effusion. Probably the excessive pressure leads to the damage of superficial areas of recent disease in the lung especially if adhesions be attached there. Peters and Wooley (18), suggest that adhesions pulling on superficial thin-walled cavities may lead to cavity rupture and fluid formation, but this will, they say, usually be purulent.

Concerning the introduction of air when

inadequate manometric oscillations have been obtained, it may be noted that in this hospital resident doctors are instructed to obtain a free swing of at least five divisions on the manometer before air is introduced. In addition, air is introduced with the tube leading to the manometer open, so that if the attempt to introduce air too rapidly is made, fluid will be blown out of the manometer. These two factors can therefore be considered to be unimportant so far as the present patients are concerned.

Thoracoscopy was performed in twelve patients in each of Groups Y and Z and in each group six of these patients developed an effusion at some date afterwards. One patient in Group Y (43, J.B.) previously had a small effusion which was negative for tubercle bacilli and had disappeared before operation.

TABLE 18. GROUP Y.

No. and Initials.	Duration between thoracoscopy and effusion (in months)
3. M.P.	10¼.
13.G.McC.	3¼.
15. E.W.	Fluid developing when thoracoscopy was done. It became turbid four months later.
40.M.M.	4¼.
43.J.B.	1¼.
44.M.T.	1½.

TABLE 18. GROUP Z.

No. and Initials.	Duration between thoracoscopy and effusion (in months).
6. A.R.	$2\frac{1}{2}$.
18. M.A.	3.
19. M.A.	$9\frac{1}{2}$.
22. S.S.	1.
23. M.W.	4.
25. M.McA.	$3\frac{1}{2}$.

In only three patients in Group Y (15, 43, 44) and in one patient in Group Z (22), could the thoracoscopy have had any immediate bearing on the development of an effusion. Only two of these four patients had adhesions cut (15, 43) and in only one (44), did the fluid not become purulent. No secondary infection was found in any fluid. Weisman (15), states that "an effusion usually follows the intentional severance of a pleural band as in pneumolysis," and Mistal (38), finds seventy to eighty per cent. of exudates after pneumolysis, of which only ten per cent. are large. He believes that pleurolysis stimulates the resorption of pre-existing effusions in half of the cases operated. By good technique and proper selection of patients he thinks that the incidence of empyemata can be reduced to two per cent. Dufault and Laroche (39), also report a

low/

low incidence of empyemata following adhesion section (0.5%). Ustvedt (30), quotes Gullbring who performs pneumolysis in sixty to eighty per cent of recently induced artificial pneumothoraces, and in five hundred and thirty-one cases he reports only ten large effusions, 1.88%. Goorwitch (19) reports thirteen per cent of serous effusions following ninety-seven intrapleural pneumolyses; this excludes small transient effusions. Following eight per cent of the operations, an empyema resulted, this being preceded by a serous effusion in twenty-two patients. On reading Goorwitch's review of the literature on this subject, one is impressed by the variation in the post-operative interval regarded by different workers as significant. One worker, Smart, regards empyemata occurring one month to two years after operation as possibly related to it. Wollaston (26) reports an incidence of 19.5% of pleural effusions following two hundred pneumolyses, 2% of tuberculous empyemata and 0.5% of mixed empyemata. As noted previously, he is prepared to operate even in the presence of an acute pleurisy in order to lessen the strain imposed on diseased areas of lung by adhesions. He believes that operation is not responsible in the large majority of patients for any empyema that may follow/

follow it. In the writer's series of fifty patients having effusions, four developed an empyema at some time following thoracoscopy, no fluid being present at the time of operation; another four patients having a serous effusion at the time of operation later developed an empyema; and in two patients an empyema present before operation persisted after it. The time interval between operation and the first occasion on which purulent fluid was observed is given for each patient in the following table.

TABLE 19.

Group	No. and Initials.	Duration in months between thoracoscopy and empyema formation.
Y	43.J.B.	1. No effusion present at operation.
Z	6.A.R.	6. No effusion present at operation.
Z	22.A.S.	1½. No effusion present at operation.
Z	25. M.McA.	6. No effusion present at operation.
Y.	15.E.W.	4. Serous effusion present at operation.
Y.	23.M.B.	3. Serous effusion present at operation.
Y.	39.M.F.	3. Serous effusion present at operation.
Z.	11.A.H.	7. Serous effusion present at operation.

It is possible that in all of these patients the operation had some influence on the development of an empyema; No. 22 of group Z was the only patient in whom thoracoscopy without pneumolysis was performed. The incidence of empyema following thoracoscopy and pneumolysis was therefore fourteen per cent. in this series, a significant increase on the figures given by Goorwitch and Wollaston. This is a finding of considerable practical importance and lends support to the statement made by Benjamin (40) that "thoracoscopy should not be done during an acute pleurisy." Jacobaeus (41) believes that if a patient has a serous pleurisy before operation the outlook is not so favourable because such pleurisies usually become worse after the surgeon's intervention. Chandler (42) also pointed out the possible dangers of tuberculous empyema and spontaneous pneumothorax if large complicated adhesions are subjected to cauterisation. The patients in Group Y (15, 23, 43) all had acute pleurisies at the time of operation and large adhesions were divided in each case. The heat of the lamp or the perforation of parietal tubercles by the cannula may also have had some effect in producing these effusions, especially when no adhesions were cut, as in Group Z No. 22. It may be concluded then that thoracoscopy and pneumolysis definitely/

definitely have some influence on the development of pleural effusions and more especially empyemata.

Further factors predisposing to pleural effusions are given in the following paragraphs.

(2) Exercise.

Both Burrell (32), and Wingfield (31), state that exercise has not, in their experience, been a predisposing cause of pleural effusion during artificial pneumothorax. It has already been demonstrated in Table 9b, that in the writer's series 56% of effusions occurred within the first three months of treatment, a time during which practically every patient was confined strictly to bed. By the end of six months from the start of treatment, 72% of the patients had an effusion, and at this time exercise, if permitted, was still markedly restricted, the patient being up for only one to two hours per day. It may be presumed that exercise was of little importance in this group of patients as a factor in the causation of a pleural effusion.

Gemmill (43), in a personal communication, points out that in a series of artifical pneumothoraces conducted entirely from tuberculosis clinics in Glasgow, the incidence of pleural effusions was particularly low. 24% of patients had a trace of fluid only/

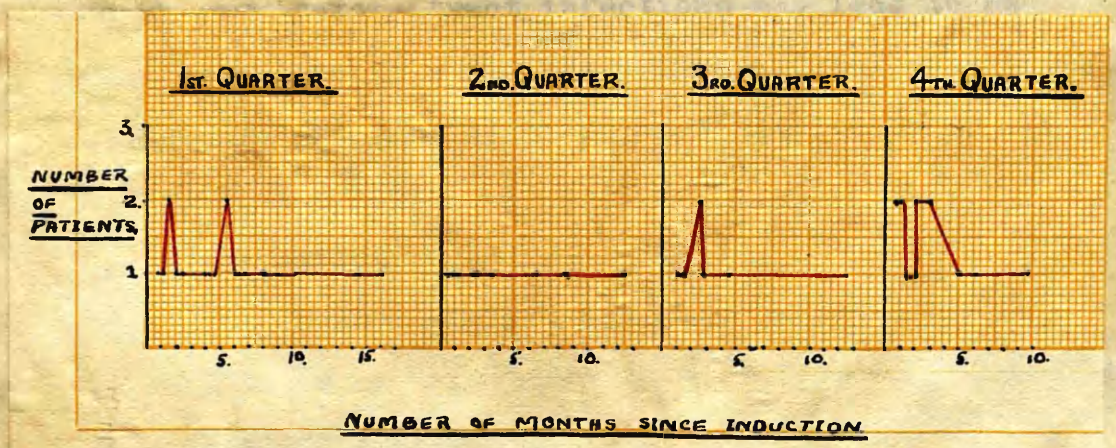
only, 8.67% had effusions of moderate degree and 2% had large effusions. Only one empyema was found. These patients, however, suffered usually from comparatively small lesions. This in itself would account for the figures quoted, but the fact that such happy results were achieved by out-patient treatment alone is interesting.

3. Season and Intercurrent Infection.

	Group Y.		Group Z.	
	No.	%.	No.	%.
Patients developing an effusion in first quarter of year.	10.	40.	9.	36.
Patients developing an effusion in second quarter of year.	7.	28.	4.	16.
Patients developing an effusion in third quarter of year.	2.	8.	5.	20.
Patients developing an effusion in fourth quarter of year.	6.	24.	7.	28.

It is noticeable that 64% of the effusions in each group occurred during the months of October to March of the following year. This is in accordance with Peters' and Wooley's findings. Burrell (32), however, is quite emphatic in stating that weather has little/

little influence on the causation of pleural effusions and Weisman (15) also found little seasonal variation. Some authors believe that intercurrent infections predispose to pleural effusions in pneumothorax patients, and the fact that in this series the highest incidence of effusions fell during the winter months of the year, when minor infections are most common, may lend some support to this idea. Tuberculous meningitis has a similar seasonal incidence in children, (Paterson, 44). However, before definitely incriminating any particular season of the year, it is well to consider the duration of pneumothorax treatment before the onset of an effusion in relation to season. This may be demonstrated by the following graphs.



It is evident from the graphs presented, that in each quarter of the year, the majority of effusions occurred within the first six months of treatment, a period during which it has been previously demonstrated that they are most likely to occur. This being so, it may be taken that on the whole the season of the year is, per se, of little importance.

In Group Y, only four patients had recent intercurrent infections before the onset of their pleural effusions. Each of these patients had an attack of coryza at intervals of one, three, four and five weeks respectively before the effusion was noted. The patients in Group Z were not specially questioned on this subject. It would seem that upper respiratory tract infections may lead to an acute pleurisy in a few patients by diminishing their resistance and thus allowing an exacerbation of the tuberculous process.

4. Menstruation.

Menstrual hyperaemia is believed by some workers to be of importance in the causation of effusions in pneumothorax patients, (1). Of the patients in Group Y, twenty-three were women and of these only four menstruated within a period of five days before or after the onset of an effusion. No notes are

available for Group Z patients. It would appear that in this series menstruation had little bearing on the occurrence of an effusion.

5. The Gas.

All patients received air at room temperature and it cannot be stated what influence any other gas might have had in preventing an effusion. Burrell (32) finds that the gas employed matters not at all, nor does heating the air as it is given have any beneficial effect. Portas and Corralo (45) using ozone instead of air , found no effusions in a series of forty-two artificial pneumothoraces.

6. Allergy.

By allergy is meant the difference in response of the body to a second dose of an antigen compared with its response to the first dose (46). The second reaction may be stronger or weaker than the first; if it is stronger, allergic hypersensitivity is said to be present, and if weaker, allergic immunity is present. Paterson (47) found that if he introduced virulent tubercle bacilli into the pleural cavity of normal guinea-pigs, no effusion of demonstrable proportions appeared, but it did appear if the guinea-pigs were previously sensitised by subcutaneous inoculation of tubercle bacilli. Howard and De Veer (48) found that the more heavily infected is/

is the guinea-pig, the more extensive and severe is the allergic serositis which occurs. Petroff and Stewart (49) and Montgomery and Lemon (50 and 51) have confirmed the work of Paterson. However, Lemon and Feldman (52) using rabbits sensitised by the subcutaneous injection of 0.1 mgm. of bovine tubercle bacilli, discovered that subsequent intrapleural injections of potent old tuberculin did not produce a pleural effusion or any demonstrable lesions on post-mortem examinations of the pleura. They suggest that the old tuberculin may have been absorbed so rapidly that an effusion had not time to form. They had previously demonstrated that when virulent bovine tubercle bacilli were injected into the pleural space of normal rabbits, a transitory small effusion formed but disappeared in two or three days. However it reappeared in about two weeks and progressively increased and persisted till the animal's death from tuberculosis. They therefore postulated that in such animals all the bacteria introduced were not removed by the lymphatic vessels but that they increased greatly in numbers and acting as particulate foreign bodies brought about a recurrence of exudation. They state "it would seem probable that the bacteria themselves must remain in the pleura or be added constantly to the pleural fluids to produce an effusion," (52). In the course

of experimental tuberculosis they have seen evidence which convinced them that tubercle bacilli were liberated from ulcerating subpleural tubercles into the pleural cavity and in such animals a pleural effusion occurred.

All the patients in the present investigation suffered from tuberculosis and it has been demonstrated that 92% of the fifty effusions investigated showed tubercle bacilli. It is not unreasonable to postulate that allergy played as important a part in these human subjects as it did in the experimentally produced effusions in guinea-pigs and rabbits. Wingfield (53) notes that the tissues which are close to a focus of previous disease appear to be more allergic than those further distant. Baum (54) quotes Neumann of Vienna, who states that the amount of fluid formed during artificial pneumothorax treatment can be reduced to a minimum by the systematic use of tuberculin in every case. Baum, himself, believes that some form of specific treatment is indicated when an appreciable amount of fluid has formed during artificial pneumothorax therapy. Allergy, then, cannot but be considered to be of practical importance in the causation of the effusions of artificial pneumothorax.

7. Miscellaneous factors.

(a) Circulatory disturbance.

Disturbance of the circulation within the chest would seem to be of little importance except in so far as too sudden compression of a diseased and congested lung may lead to excessive passive congestion. Rao (14) advances this theory, but Alexander (10) quotes several workers who have shown that the collapsed lung contains less blood. This pleural fluid should however be a transudate. Complete collapse of a non-tuberculous lung by spontaneous pneumothorax does not give rise to a pleural effusion.

(b) Calcium deficiency.

Pisani and Smejkal (55) have suggested that calcium deficiency may play a part in the aetiology of these effusions. The writer did not employ any drugs in his series with a view to preventing effusions and cannot confirm the suggestion made above. Foulis (56), in a personal communication, reports that the administration of calcium by mouth or by injection is of no value in preventing effusions during pneumothorax therapy.

(c) Phrenic crush.

None of the fifty patients examined had a phrenic crush done on the same side except one in Group Z, (14, R.H.), who had this operation performed four months after having had a small effusion which showed tubercle bacilli and which disappeared after

one aspiration. The writer does not know whether this operation would materially reduce the incidence of effusions. Lilienthal (57) quotes Sauerbruch who believes that phrenic crush is beneficial in preventing the formation of effusions. Sauerbruch has found that resorption and exudation diminish after resection of the phrenic nerve.

Small Transitory Effusions.

It is the belief of most workers in the field of artificial pneumothorax, that in practically every patient, if observation by fluoroscopy be carried out very frequently, small transitory collections of fluid in the costo-phrenic sinus and insufficient to cover the hemi-diaphragm, will be seen. Gloyne (2) states that "small quantities of fluid are present in practically every case of spontaneous or induced pneumothorax." According to Davies (11) some authorities believe that if artificial pneumothorax be continued long enough, 100% of patients will show an effusion which is often transient and can only be detected by radiological examination. Dumarest is quoted by Packard, Hayes and Blanchet (1) as referring to these small effusions under the heading "Benign Pleurisy" in contradistinction to "Tuberculous Pleurisy."

Other/

Other writers classify them among what they term "cold effusions." Among such investigators may be mentioned Rao (14) and Zavod (58). It was previously noted that many of the effusions which occur during artificial pneumothorax therapy have the characters partly of transudates and partly of exudates. Mayer and Dworkin (59), however, state that "undoubtedly the great majority of pleural effusions complicating artificial pneumothorax are transudates. Studies in several series of cases show that 70 to 80% do not reach much above the upper level of the costo-phrenic sinus. Small transient puddles of fluid lasting a few days or more are present in most cases at one time or another." Rosenthal (34) found that puddles occurred in 33% of fifty-four artificial pneumothoraces and that these puddles might persist for days, weeks or months. Ford (24) found an even smaller percentage of puddles. In his series of forty-six pneumothoraces only 12% had transient effusions. The writer found 16% of puddles in his series of fifty patients, 8% occurred in patients whose pneumothorax was not complicated by a typical tuberculous effusion and 8% occurred in patients who later had a tuberculous effusion. One of the latter group showed all the clinical signs and symptoms of

an/

an acute exacerbation of tuberculous disease when the large effusion occurred, although no tubercle bacilli were recovered from it. Undoubtedly the low percentage figure recorded in the present series is due to the fact that, on the average, only fortnightly screen examinations were possible in this group because of pressure of work. Stivelman and Rosenblatt (60) state that, "these effusions are of no consequence, do not affect the intrapleural pressure, need no special treatment and that insufflations should be given as if there were no effusion." They note that no acute symptoms accompany their presence but Rosenthal (34) found a rise of temperature in one patient at the time when a puddle appeared. Mayer and Dworkin (59) quote Cloetta who showed that the microscopical appearance in collapsed lungs suggested capillary engorgement. They also quote Christie, whose finding of a diminished distensibility and marked rigidity in the lungs of pneumothorax treated patients, they use to explain the occurrence of transudates in such patients. They believe that the rigidity of the lung is similar to the pulmonary congestion and oedema found in congestive cardiac failure, a condition in which transudates are not infrequently found in the pleural space. They believe also that there is no reason why the normal amount/

amount of fluid present within the pleural space should increase during pneumothorax treatment. In their opinion, too sudden pulmonary compression, and sudden and excessive fluctuations in intrapleural pressure are prone to cause the appearance of fluid within the pleural space.

The writer has been unable to find in the literature any detailed analysis of these small accumulations of fluid, no doubt because of the difficulty of obtaining sufficient for adequate examination. Mayer and Dworkin (59) state that "the fluid seen after the establishment of most pneumothoraces is a limpid serous filtrate, containing little fibrin, protein or cells." Of the eight patients in whom a puddle was noted by the writer, in four, it was possible to obtain some fluid for examination. Six of these puddles occurred in right pneumothoraces and two in left pneumothoraces. Of the larger effusions occurring in the group of fifty patients, 44% were on the right side in Group Y and 56% in Group Z. Thus the percentage of 75% for puddles occurring on the right side is considerably higher than the figures for the typical effusions. This is not/

not surprising, for, if an effusion be tuberculous, as was proved in the majority of patients in Groups Y and Z, then it will arise with equal facility in the right or left pleural cavity. Gloyne (2) points out, however, that transudates are more liable to form in the right pleural cavity in patients with cardiac failure because of the pressure of the dilated right auricle on the great azygos vein and superior vena cava. It may be that the increased resistance occurring in the pulmonary circulation in patients having pneumothorax treatment, can cause some degree of dilatation of the right auricle with a resultant collection of fluid in the right pleural space. The writer's findings will now be presented.

TABLE 21. GROUP X.

CLINICAL FINDINGS IN PATIENTS DEVELOPING PUDDLES.

No. and Initials.	1. H. W.	12. W.J.	20. M.McH.	37. A.V.
Side.	Right.	Right.	Right.	Left.
Time after induction. (in months).	4.	1¾.	4½.	5¾.
Duration of effusion.	4 days.	7 days.	14 days.	3 to 4 weeks.
Amount of effusion.	1 fb.	3 fb. 45 ccs.	1 fb.	3 fb. 80 ccs.
Intrapleural pressure.	A.P. abandoned before puddle appeared.	no change	A.P. abandoned before puddle appeared.	no change.
Group. Mod. Far Adv.	I.B.	III.B.	III.B.	III. B.
Type of disease.	Fibro-Caseous.	Fibro-Cavernous.	Caseo-Cavernous.	Caseo-Cavernous.
Adhesions.	Present.	Present.	Present.	Present.

A.P. - Artificial pneumothorax.
fb. - fingerbreadth or fingerbreadths.
Mod. - Moderate.
Far adv.-Far advanced.

TABLE 21. GROUP Y.

CLINICAL FINDINGS IN PATIENTS DEVELOPING PUDDLES.

No. and Initials.	3. M.P.	14. E.S.	34. A.McN.	45. M.R.
Side.	Left.	Left.	Right.	Right.
Time after induction. (in months).	6.	2½.	2¾.	9.
Duration of effusion.	6 days.	21 days.	21 days.	7 days.
Amount of effusion.	1 fb. 3 ccs.	3 fb. 70 ccs.	2fb.	1 fb.
Intrapleural pressure.	no change.	no change.	tendency to pos. readings after refills.	no change.
Group. Mod. Far adv.	B.	C.	II. C.	A.
Type of disease.	Caseo-Cavernous.	Caseo-Cavernous	Fibro-Cavernous.	Caseous.
Adhesions.	Present.	Present.	Present.	Present.

fb. - fingerbreadth or fingerbreadths.

pos. - positive.

Mod. - Moderate.

Far adv. - Far Advanced.

The puddle in the patient (3. M.P.), occurred immediately after a thoracoscopy.

It is seen from Table 21 that there is a range of seven weeks to nine months from the time of the induction of artificial pneumothorax till a puddle appeared. However, as noted in the section dealing with the larger effusions, the majority appeared within the first six months. Again, the duration of the period during which the puddles persisted was always short and this is in accordance with the findings of several of the workers quoted. No puddle persisted for months as was found by Rosenthal (34). The amount of fluid present was usually very small thus making aspiration most difficult. In four patients only, were specimens of fluid obtained. It should be mentioned here, that not one patient showed clinical signs or symptoms of the development of fluid within the chest. No. 37, A.V. had a rise of temperature to 99° F. six days before fluid was noted on screening, but this could have been due to a contralateral dry pleurisy which was at that time present. In one patient alone, was there any significant alteration in the intrapleural pressure. The manometer readings showed a positive swing after refills, but the mean reading was usually on the negative side. On one occasion it was + 2.

These puddles occurred in patients with moderately/

moderately advanced disease and far advanced disease. In addition, all types of disease from caseous to fibro-cavernous were noted, although the majority of patients had the more acute types. It will be of interest to consider next the laboratory findings where it was possible to obtain fluid for examination.

TABLE 22. LABORATORY FINDINGS.

No. and Initials.	3. M.P.	12. W.J.	14. E.S.	37. A.V.
Amount and character of fluid.	3ccs. of blood-stained fluid.	45ccs. of blood-stained fluid.	70ccs. of blood-stained turbid fluid.	80ccs. of turbid yellowish blood-stained fluid.
Specific gravity.	not done.	1014.	1020.	not done.
Esbach percentage.	not done.	4.0%.	1.8%.	3.5%.
Smear for tubercle bacilli.	negative.	negative.	negative.	negative.
Culture for tubercle bacilli.	negative.	negative.	negative.	negative.
Guinea-pig inoculation for tubercle bacilli.	negative.	negative.	negative.	negative.

All/

All fluids examined gave a positive Rivalta's reaction; none of the fluids showed any organisms on examining a film prepared by Gram's method and none gave a growth on culture in Glucose broth.

It is noticeable that all fluids examined were blood-stained. This could be accounted for by a preceding thoracoscopy in patient(3, M.P.), but none of the other patients had thoracoscopy performed before the puddle appeared. Diapedesis of red cells could possibly account for this characteristic of the fluids examined.

Rivalta's test is positive if the fluid in which it occurs is an exudate, Gloyne (2). Although this test was positive in all the fluids examined, the specific gravity and Esbach readings did not always agree in indicating that the fluid was an exudate. However, as Gloyne (2) notes, the method of estimating the percentage of protein by the Esbach method, which he describes, is only a rough one. As no specific gravity beads were available, the specific gravity had to be estimated by dilution of some of the fluid and a reading taken by an hydrometer. Thus both these physical findings are of little value.

Much more important are the negative bacteriological findings. No evidence of tubercle bacilli was found in any fluid by any of the methods

which/

which yielded such satisfactory results in the larger effusions. Nor was there any evidence of secondary infection.

Conclusions.

1. Pleural effusions which develop during artificial pneumothorax treatment may be small transient collections of fluid or larger and more persistent in nature. The former are of little importance, whereas the latter are associated with the more serious complications of artificial pneumothorax therapy.

2. The transient puddles are probably exudates but they are not tuberculous in origin. The larger serous effusions are certainly due to invasion of the pleural cavity by tubercle bacilli which can be demonstrated in a very high proportion of these effusions by careful technique. The cytology of these effusions confirms their tuberculous nature.

3. Tuberculous effusions occur most often in patients suffering from advanced and acute pulmonary tuberculosis. In this series the shorter the duration of the patients' history the more often did effusions occur.

4. Tuberculous effusions frequently occur in the early months of treatment and their aetiology is closely associated with the presence of recent subpleural tubercles and large and complicated adhesions. The

shedding of tubercle bacilli into an allergic pleural cavity is the trigger mechanism which initiates these effusions.

5. Of the various ancillary factors considered in their causation, internal trauma as by thoracoscopy and adhesion section, and intercurrent infection, appear in this series to be worthy of consideration. These act either by producing damage to a diseased area on the lung surface or pleura, or by so diminishing the general and local resistance to the tuberculous infection, that its spread into the pleural cavity is facilitated.

The Empyemata.

There is some difference of opinion as to what constitutes a tuberculous empyema. Some writers would include any pleural fluid containing tubercle bacilli, (61), while others not only insist on frank pus being present, but include in their definition the clinical picture which accompanies its formation and subsequent course, (62). In this study Dickey's (63) definition is employed. He states merely that any sero-purulent or purulent fluid containing tubercle bacilli is, in his paper, classed as a tuberculous empyema.

Their aetiology is closely linked with that of serous effusions occurring during artificial pneumothorax therapy, for many empyemata develop from such effusions. According to Peters and Wooley (18) it was Brauer and Spengler who were among the first to observe the evolution of a clear serous effusion into an empyema. They quote also Dumarest who has investigated this problem intensely. Packard, Hayes and Blanchet (1) believe that almost always a tuberculous empyema is preceded by a serous effusion during treatment by artificial pneumothorax. Fishberg (64) notes that while effusions may remain serous for months or even years they most often change in character and become purulent should they not be absorbed.

Hayes/

Hayes (65) states that " serous effusion bears a grave relation to empyema." Leaver and Hardaway (36) found on investigating the records of seven hundred and fifty patients treated by artificial pneumothorax that 5.8% developed empyemata. Of these patients, twenty-one or 60% had a superimposed spontaneous pneumothorax and fourteen or 40% had a clear fluid, in the absence of a demonstrable spontaneous pneumothorax, before the empyema appeared. They note, however, that following a superimposed spontaneous pneumothorax with an open fistula, the pleural exudate is generally first serofibrinous in character although it soon becomes cloudy and later becomes frank pus. It is not necessary for a frank broncho-pleural fistula to exist, for Coryllos (66) has noted that a high incidence of punctiform fistulae, which quickly seal over, can give rise to pure tuberculous empyema. It has been noted in a previous section that tubercle bacilli may be liberated into the pleural space by ulceration of a subpleural focus through the visceral pleura, by rupture of the wall of a cavity, or by the tearing of an adhesion. Many workers have found that

empyemata/

empyemata are prone to occur in mechanically unsatisfactory pneumothoraces. Among such may be mentioned Goorwitch (64), Dickey (63), Cutler (67), Weisman (15), and Shields (68). Leaver and Hardaway (36) state that post-mortem findings show that the site of rupture of subpleural lesions is most often near the pulmonary attachment of pleural adhesions. Gordon (69) quotes Alexander, among other writers, as noting that tubercles of the pleura are often found in considerable numbers at the base of adhesions. It is obvious that the tension put on such adhesions by large refills of air and coughing, may so damage the lung at the pulmonary attachment of an adhesion, that tubercle bacilli may be liberated quite easily into the pleural space. It was noted in the section on the anatomy of the pleura that the lymphatic drainage from the pleural portion of the lung is towards the pleura. This, too, facilitates infection of the pleural space. Several writers are agreed that the more acute types of tuberculosis are liable to be followed by empyemata should pneumothorax treatment be attempted. Hayes' (65) patients all suffered from far advanced disease, and a higher proportion of those with more recent disease developed empyemata than/

Table 23. Group Y.

No. and Initials.	Group.	Type of Disease.	Type of empyema.	Adhesions.	Preceded by serous effusion.	Followed Operation.
15.E.W.	II.C.	Caseo-cavernous.	Tuberculous.	Presemt +.	Yes: 4 months.	Yes: 4 months.
22.A.L.	II.C.	Caseo-cavernous.	Tuberculous.	Present + +.	No.	No.
23.M.B.	II.C.	Caseo-cavernous.	Tuberculous.	Present + +.	Yes: (1) 3 months. (2) 1 month.	
29.J.W.	IV.C.	Caseo-cavernous.	Tuberculous.	Present + +.	Yes: 4 months.	No.
32.A.K.	IV.C.	Caseo-cavernous.	Tuberculous.	Present + +.	Yes: 9 months.	No.
34.A.McN.	II.C.	Fibro-cavernous.	Tuberculous.	Present +.	Yes: 5 months.	No.
36.D.M.	V.C.	Fibro-cavernous.	Tuberculous.	Present +.	Yes: 2½ months.	No.
39.M.F.	IV.C.	Fibro-cavernous.	Tuberculous.	Present +.	Yes: 7½ months.	Yes: 3 months.
42.M.W.	IV.C.	Caseo-cavernous.	Tuberculous.	Present + +.	Yes: 5 months.	No.
43.J.B.	IV.C.	Caseo-cavernous.	Tuberculous.	Present + +.	Yes: 5 months.	Yes: 3 months.
47.J.B.	IV.C.	Caseo-cavernous.	Tuberculous + Pyogenic.	Present + +.	Yes: 5 months.	No.

Table 23. Group Z.

No. and Initials.	Group.	Type of Disease.	Type of empyema.	Adhesions.	Preceded by serous effusion.	Followed Operation.
2. M.B.	II.C.	Caseo-cavernous.	Tuberculous.	Present + +.	Yes: unknown.	No.
6. A.R.	I.C.	Fibro-caseous + cavitation.	Tuberculous + Pyogenic.	Present + +.	Yes: 5 months.	Yes: 7 months.
7.C.McK.	IV.C.	Caseo-cavernous.	Tuberculous.	Present + +.	Yes: 3 months.	No.
9.H.McG.	Mod.C.	Caseo-cavernous.	Tuberculous.	Present + +.	Yes: unknown.	Present before operation.
11.A.H.	IV.B.	Fibro-cavernous.	Tuberculous.	Present + +.	Yes: 15 months.	Yes: 7 months.
12.I.M.	IV.B.	Fibro-cavernous.	Tuberculous.	Present + +.	Yes: unknown.	Present before operation.
18.M.A.	II.B.	Fibro-cavernous.	Tuberculous.	Present + +.	Yes: 14 months.	Yes: 15 months.
22.S.S.	IV.C.	Caseo-cavernous.	Tuberculous.	Present + +.	Yes: 1 month.	Yes: 2 months.
25.M.McA.	Mod.C.	Fibro-cavernous.	Tuberculous.	Present + +.	Yes: unknown.	Yes: unknown.

Present + = Few adhesions.

Present + + = Multiple adhesions.

Table 24.

SUMMARY OF TABLE 23. Group Y. :- 11 patients.
Group Z. :- 9 patients.

	Group Y; No. of patients.	Group Z; No. of patients.
Classification. Moderately advanced.	0.	2.
Far Advanced. I.	0.	1.
Far Advanced. II.	4.	2.
Far Advanced. III.	0.	0.
Far Advanced. IV.	6.	4.
Far Advanced V.	1.	0.
Symptom Group. Group A.	0.	0.
Group B.	0.	3.
Group C.	11.	6.
Type of disease. Caseo-cavernous.	8.	4.
Fibro-cavernous with cavitation.	0.	1.
Fibro-cavernous.	3.	4.
Adhesions. Present +.	4.	0.
Present + +.	7.	9.
Preceeding serous effusion.	10.	9.
Attributable to operation.	1.	1.

Only/

Only one patient, Group Y (47. J.B.), had a frank bronchopleural fistula.

One patient, Group Z (6. A.R), had a tuberculous empyema later contaminated by Staph. albus by the operator during aspiration. Eleven patients of Group Y and nine patients of Group Z developed empyemata, thus giving an incidence of 40% for the fifty patients having effusions. The incidence of empyemata in the fifty pneumothorax treated patients of Groups X and Y is 22%, a figure which is somewhat above the average. The incidence given by a few other workers is shown below.

TABLE 25.

Name.	Number of patients.	Incidence.
Leaver and Hardaway (36).	750.	5.8%
Unverricht quoted by Ustvedt (30).	2893.	1.1%
Matson, Matson and Bisaillon (28).	480.	12%
Nalbant (71).	20.	35%
Dumarest quoted by Packard, Hayes and Blanchet (1).	247.	17%
De Cecio and Potter (62).	184.	12%

The/

The high incidence in the writer's series is due undoubtedly to the large number of patients having advanced tuberculosis. It is notable that of all the patients in Group Y and of seven of the nine patients in Group Z who developed empyemata, the majority fell in the most far advanced groups of Salkin and Cadden's classification. In addition, all of these patients suffered from considerable constitutional upset on admission to hospital, twelve out of the twenty having an acute type of the disease. These findings coincide with the reports given by other workers previously quoted.

It has been mentioned that most pneumothorax operators find that empyemata are prone to occur in ineffective pneumothoraces. This too is the writer's experience, for all of the twenty patients developing empyemata had also adhesions present which were so large in all but four patients as to make the pneumothorax only partially effective. In these four patients the adhesions were cut, one patient requiring two sessions for the operation. On the other hand, the findings of Matson, Matson and Bisaillon (28) that fifty per cent. of their empyemata occurred in satisfactory pneumothoraces cannot be ignored.

Doubtless/

Doubtless, involvement of the visceral pleura by recent tuberculous infiltration could account for this. Of four patients in Group Y on whom thoracoscopy was performed, three showed pleural tubercles involving the visceral pleura. Of seven patients in Group Z, three showed pleural tubercles but no special note was made by the operator in three of the four remaining patients as to whether tubercles were present or not. When tubercles were seen, they were present in considerable numbers, except in one patient. It may therefore be taken as proven that in every patient who developed a tuberculous empyema the pleura was involved by disease of some duration. This was indicated by the presence of adhesions. In addition, several patients showed evidence of recent involvement of the visceral pleura in the form of visible tubercles.

In every patient except one, Group Y, (22, A.L.) empyema was preceded by serous effusion. One patient, Group Y (47,J.B.), developed a bronchopleural fistula which was followed by a secondarily infected empyema. Prior to the development of the fistula, she had a serous effusion which had shown no tendency to become purulent. Excluding patients (22, A.L. and

47, J.B/

47, J.B) of Group Y, 81% of empyemata were preceded by serous effusions, all positive for tubercle bacilli. Leaver and Hardaway (36) treated two hundred and fifty patients with an initial serofibrinous exudate and of these, only 23.6% became purulent. They also found that thirty-five patients from a series of seven hundred and fifty artificial pneumothoraces, developed empyemata. Of these thirty-five only fourteen or 40% developed from clear fluid in the absence of demonstrable spontaneous pneumothorax, whereas twenty-one or 60% were preceded by signs of a spontaneous pneumothorax. Goorwitch (64) describes the treatment of twelve patients with empyemata all of which were preceded by serous effusions. Packard, Hayes and Blanchet(1) state "tuberculous empyema almost always is preceded by or develops from a serous effusion." Alexander (10) notes that pure tuberculous empyema may occur at any time during pneumothorax therapy, but that in patients suffering from acute exudative or pneumonic tuberculosis it may appear soon after the induction of pneumothorax. In these patients the fluid is usually purulent from its onset or becomes so rapidly. Empyemata which occur later in the treatment are however usually preceded by serous effusions. It is to the latter group that practically all the writer's patients belong. Alexander continues that the time which a serous effusion takes to change

into pus is variable but that it may occur within three months. In the writer's series the shortest time taken for this change was one month and the longest time was fifteen months. Most patients developed an empyema three to five months after the onset of a serous effusion. It would appear that serous effusions are prone to give rise to empyemata during the course of pneumothorax therapy and it is therefore important to determine whether any significant differences in the clinical findings are evident in those patients who developed an empyema consequent to a serous effusion. If appreciable differences were found, it might be possible to modify the treatment with the object of avoiding the otherwise inevitable empyema.

A summary of the findings at the onset of the serous effusion, as derived from Table 10, is next given for those patients who developed empyemata excluding (22, A.L.) and (47, J.B.) of Group Y for reasons previously explained.

Table 26. Group Y:- 9 patients. Group Z:- 9 patients.

	Group Y. No. of patients.	Group Z. No. of patients.
Constitutional upset.		
Present.	7.	4.
Absent.	2.	5.
Dyspnoea.		
Present.	6.	4.
Absent.	3.	5.
Pain.		
Present.	7.	3.
Absent.	2.	6.
Cough and spit.		
No change.	5.	6.
Increased.	4.	3.
Weight.		
Increased.	1.	1.
Fell.	3.	3.
Bed Patient.	3.	3.
No change.	2.	2.
Fever (one unknown).		
Absent.	1.	2.
Mild.	1.	3.
Moderate.	6.	3.
Severe.	1.	0.
Blood Pressure.		
No change.	4.	unknown.
Fall...mild.	1.	unknown.
Fall...moderate.	3.	unknown.
Fall...severe.	1.	unknown.
Amount of effusion.		
Small.	1.	1.
Moderate....	1.	6.
Large.	7.	2.

A scrutiny of the above table reveals that the respective positive and negative findings for the two groups tend to cancel out each other. In Group Y symptoms and signs were more pronounced than in Group Z and a majority of the patients in the first group had large effusions. It was rare for a small effusion to give rise to an empyema. Fever was usually present and tended to be marked in most patients. The clinical findings which were in Group Y patients closely observed during the course of the serous effusion, indicated only in two patients (36, D.M.) and (43, J.B.) an unfavourable change. Their condition progressively deteriorated, their temperature and pulse charts being unsatisfactory. Both however had bilateral disease.

It was thought that the cytological and bacteriological examinations of the serous effusions themselves, might be of more value in determining which of them would become purulent. In the following table the neutrophil percentage is considered for the two groups.

A:- serous effusions not becoming empyemata.

B:- serous effusions becoming empyemata.

The results of direct smear examination for tubercle bacilli are also given. It should be noted that the results given here refer to the first examination of the fluid only and (22, A.L.) and (47, J.B.) of

Group/

Group Y are again omitted from the empyema group.

TABLE 27. GROUP Y.

	Group A.	Group B.
No. of patients.	14.	9.
Neutrophil percentage.		
0 - 25.	5.	2.
25 - 50.	7.	4.
50 - 75.	1.	1.
75 - 100.	1.*	2.
Tubercle bacilli		
Absent.	7.	2.
+	4.	3.
+ +	2.	2.
+ + +	1.	2.

* This was a late specimen but the first obtained by the writer.

It is evident from Table 27 that a greater number of patients whose fluid did not become purulent had a low neutrophil count in the first specimen of fluid to be examined. In only two patients did the neutrophil percentage rise in the subsequent fluids obtained. In the empyema group, there were relatively more patients having an increased neutrophil percentage in the first specimen/

specimen of fluid examined, and in all patients of this group, the neutrophil percentage rose on subsequent examination of the fluid. In general, the neutrophils increased as the fluid became turbid, reaching their maximum when it was frankly purulent.

Tubercle bacilli were detected in 77.7% of serous effusions later becoming purulent, and in 50% of serous effusions not so doing, on the first examination. Both patients of Group B whose fluid was negative on the first examination, later showed tubercle bacilli in the fluid, whereas two of seven patients of Group A with the initial examination negative for tubercle bacilli, did not later develop a tubercle positive effusion. Tubercle bacilli tended to increase in number on direct smear examination as the serous effusion became turbid, but in effusions remaining serous they increased in number only to a small extent. In a few patients subsequent direct smear examinations were negative in the serous effusion group. Of the patients in Group Z who developed empyemata, all that can be said is that as these patients were usually selected at random, the time interval between the onset of an effusion and the specimen examined by the writer was variable, thus producing inconsistent results. However, it may be noted that all direct smears, except two, showed

tubercle/

tubercle bacilli in this group of nine patients developing empyemata. These two negative fluids were positive by guinea-pig inoculation although not by culture, and it should be noted that one was aspirated six days after the onset of the effusion and the other at twenty-one days. It was the writer's experience that tubercle bacilli were sometimes extremely difficult to find in specimens of pleural fluid taken immediately after its appearance. In four of the nine specimens of group B, tubercle bacilli were numerous on direct smear examination.

It would seem that repeated examination of the effusion to discover its macroscopic appearance, the nature of the predominating cells and the number of tubercle bacilli, will offer the best means of assessing whether an empyema will follow from a serous effusion. This procedure involves practically no risk to the patient, consumes comparatively little time compared with that occupied by clinical examinations and serial blood counts, and is certainly the most precise method of assessing the nature of the effusion. In several patients the treatment can be promptly modified at the turbid stage to try and avoid the dreaded complication developing. Packard, Hayes and Blanchet (1) found that in thirty-two patients with mild/

mild empyemata, the transition to pus was not recognised clinically in twenty-eight. As will be seen in a subsequent section, the blood picture was of no assistance in determining this change in the writer's series.

No adequate account has yet been given of the patient, Group Y (22, A.L.), whose empyema was not preceded by a serous effusion. She belonged to Group II C, and the type of her disease was caseo-cavernous. She had adhesions in her pneumothorax which was abandoned four months after the induction. An empyema appeared two months and ten days after induction of pneumothorax, and in the five week period preceding it, her temperature had been persistently abnormal and her pulse rapid. The temperature was remittent and intermittent in character and frequently reached 101°F. During this period, however, a contralateral dry pleurisy followed by a small effusion had occurred. The patient looked extremely unwell and it was possible that the markedly abnormal temperature and pulse chart findings were due to progression of the pulmonary disease. Rather remarkedly, she made no complaint of pain on the side on which the empyema appeared. The presence of an effusion on the pneumothorax side was detected by clinical examination and aspiration revealed it to

be/

be purulent. Fortunately its amount was small and so remained. The pleural space finally obliterated, and the patient was ultimately discharged in fair condition having chronic fibro-cavernous tuberculosis. It is felt that her empyema can be included with those developing from serous effusions under Group I of Packard, Hayes and Blanchet's (1) classification. Patient, Group Y (47, J.B.), who developed an empyema following a bronchopleural fistula belongs to Group IV of this classification which is as follows:-

Group I.	Mild or benign type.
Group II.	Severe empyemata due to the tubercle bacillus alone.
Group III.	Severe type secondarily infected at onset.
Group IV.	Purulent effusions which originate from a bronchopleural fistula.

The findings presented up to this point indicate that empyemata occurring during artificial pneumothorax therapy are prone to develop in patients suffering from advanced and acute pulmonary tuberculosis, whose pneumothoraces are often ineffective, and whose pleural space has been invaded by tubercle bacilli, which in most instances give rise to a serous effusion first. These basic conditions may be supplemented by other factors which in patients with less advanced disease/

disease and more effective pneumothoraces would not give rise to this unfortunate complication. Among such factors, Leaver and Hardaway (36) mention the indiscriminate use of positive intrapleural pressures which may produce rupture of large adhesions or exert an irritant effect on the pleura, intrapleural surgery, the use of oil for purposes of compression, pleuro-cutaneous fistulae following the aspiration of a hydrothorax, errors of aseptic technique, neglected hydrothoraces and the sudden cessation of pneumothorax treatment in patients having a considerable degree of collapse of the lung. Packard, Hayes and Blanchet (1) mention that a serous effusion may become purulent during a cold or any septic infection. In this series, the only factors among those mentioned above which might have been of importance, are the use of positive intrapleural pressures, the cutting of adhesions and the occurrence of intercurrent infections.

On examining the records of the manometer readings recorded at each refill, the writer finds that in Group Y, nine of the eleven patients who developed empyemata had markedly positive pressures used before their empyemata appeared. The remaining two patients had their pneumothoraces abandoned following the development of a serous effusion and no further

readings/

readings were taken of the intrapleural pressures. In Group Z six of nine patients had positive intrapleural pressures employed before purulent fluid appeared. One (12, I.M.) of the remaining three had usually negative intrapleural pressures after refills. His collection of purulent fluid however was extremely small. The other two patients (2, M.B.) and (22, S.S.), had their pneumothoraces abandoned after a serous effusion appeared. The influence of thoracoscopy and adhesion section on the development of pleural effusions has been considered in a previous section. To complete that section, empyemata which followed operation were considered there. It will be recalled that there was no uniformity of opinion as to what time limit should be set for the development of empyemata which might be attributable to operation. In the writer's series, the shortest period was five weeks after operation, and the longest interval recorded was seven months. One patient, Group Z, (22,S.S.), in whom no adhesions were cut, developed an empyema six weeks after thoracoscopy. The surgeon who performed all those thoracoscopic examinations was definitely of the opinion that his intervention was not solely responsible for empyema formation in any patient, but that the pleural state

was/

was the causal factor.

In five patients of the eleven in Group Y in whom empyemata appeared, a common cold preceded the change in the pleural effusion of each patient. No organisms other than tubercle bacilli were present in the purulent fluid aspirated, and the influence, if any, of the intercurrent infection would possibly be exerted by a diminution in the general resistance of the patient.

It would appear that positive intrapleural pressures and intercurrent infections may have had some influence on the development of empyemata in this series of patients. It is well known that positive intrapleural pressures often occur when refills of air are given to a patient with a hydropneumothorax. Therefore, the writer feels that positive intrapleural pressures are, in most instances, a result of the physical conditions present within the thorax and that they cannot definitely be incriminated as an important cause of empyemata. In patients having large adhesions, positive intrapleural pressures may produce a harmful degree of tension on the lung cortex, but it is difficult to tell why patients with satisfactory pneumothoraces should develop empyemata because of the use of positive pressures. Four

patients/

patients in the writer's series belonged to the latter category, Group Y (15, E.W., 23, M.B., 39, M.F., 43, J.B.). All the evidence presented therefore leads back to the basic factors mentioned previously as the main causes of empyemata occurring during artificial pneumothorax therapy. There is one peculiarly individual factor whose influence is unpredictable. That factor is allergy. It may well be the reason why some serous effusions become purulent while others remain serous and sometimes disappear quite unaccountably while still in that state. Packard, Hayes and Blanchet (1) state that "a silent pyothorax is perhaps due to the seepage of tubercle bacilli from a subpleural focus into the pleural cavity. Probably the pleurae have been rendered very allergic by previous mild infections and a purulent effusion results." This statement is probably correct, but it essentially depends on the fact that an artificial space has been created by the physician and that to a major extent the future happenings within that space are without his control. In dealing with the causes of empyemata unconnected with artificial pneumothorax, Price (72) notes that occasionally the pus aspirated is sterile. When this is so, the empyema is generally due to the

tubercle/

tubercle bacillus or to pneumococci which have died out. This indicates then, that tuberculous empyemata are rare apart from artificial pneumothorax.

Conclusions.

1. Tuberculous empyema is due to the peculiar conditions created by artificial pneumothorax.

2. It is most frequent in patients suffering from advanced and acute pulmonary tuberculosis and who consequently often have only partially effective pneumothoraces.

3. It could be avoided by a better selection of patients for pneumothorax therapy or by the prompt cessation of refills in patients with ineffective pneumothoraces.

4. Repeated aspiration of serous effusions is the only sure method of detecting empyemata which sometimes follow them.

5. In view of the above findings, it is probably advisable that any patient treated by artificial pneumothorax who develops an empyema, should have the pneumothorax abandoned immediately and that steps should be taken to procure rapid closure of the intrapleural space.

THE INVESTIGATION OF THE BLOOD.

The Erythrocyte Sedimentation Rate.

A great volume of work has been done in the present century on the behaviour of sedimenting blood, but it must not be forgotten that the ancients had noted the sinking of red cells of drawn blood, leaving above a buff-coloured layer which they termed the "crusta sanguinis" or "buffy coat," (73). Fahraeus (74) in 1921, gave an historical review of blood sedimentation in a paper dealing also with the results of his own research work. Among the workers whom he mentions are Sydenham, who noted that in acute diseases such as pleurisy or rheumatic fever two common and constant features were fever and the presence of buffy coat in drawn blood; Hewson, who showed that the formation of buffy coat was due to some change in the blood plasma, as the corpuscles of the patients showing a considerable buffy coat sank with the same velocity as those of normal people when suspended in the same medium; Scudamore, who in 1826 reported that the fibrin content of buffy blood was increased; Nasse, who noted that although red cells sink more slowly in defibrinated than in fresh blood, they nevertheless sink more rapidly in defibrinated buffy blood than in defibrinated normal blood, thus amplifying Scudamore's observations: Pfeiffer, who in 1897 showed that increased sedimentation of red cells/

cells did not depend on differences in specific gravity between plasma and cells, and that reduced viscosity could not be inferred from an increased rate of sinking. It had also been observed by Blundell in 1828, that in pregnant women the blood showed the presence of buffy coat. Fahraeus (74) amplified this observation in pregnant women and he endeavoured to detect pregnancy by means of the erythrocyte sedimentation rate. Rest (75) states that Fahraeus was unaware that Biernacki had reported in 1897, sedimentation tests done on 75 patients, and that his results had been confirmed by Muller and Marcano in 1898 and in 1901 respectively. In 1920, Westergren (76) described his method of performing this test and gave a review of his experience in its application to patients suffering from pulmonary tuberculosis. Various workers have, since that time, modified the methods used in the performance of erythrocyte sedimentation tests, the most outstanding being Linzenmeir, 1925, (77), Cutler, 1929, (78), and Wintrobe, 1933, (79). In 1939, Day (80) suggested expressing the result by the calculation of a "sedimentin index," this being the logarithm of the maximum velocity of sedimentation expressed in millimetres per 100 minutes. A multitude of workers of all nationalities have contributed, during the present/

present century, a wealth of information which has resulted in the better understanding of:-

1. the factors involved in the sedimentation of blood.

2. the precise clinical value which can be attached to the laboratory data obtained by this method.

Factors involved in the sedimentation of blood.

Robins (81) divides the factors affecting blood sedimentation into two main groups:-

1. Factors whose influence is exerted directly on the components of the blood.

2. Factors which modify the physiological state of the patient and affect only indirectly the elements of the blood.

Group 1.

(a) Red Blood Cells.

In 1921, Westergren (76) stated that he had found that "on the whole, no influence was exerted on the blood sedimentation rate by the number of red blood cells per cubic millimetre." He further stated that "the factor of the plasma proteins is probably of such predominant importance that the influence, itself not significant, of the changes in the relative number of red /

red blood cells generally found, when compared with the influence of the plasma proteins, becomes inconsiderable." It is widely suggested now that anaemia is a factor to be reckoned with in the performance of sedimentation tests, and, in fact, tables have been constructed enabling a correction to be applied for anaemia, (82). This may be applied in terms of the packed cell colume, as in Wintrobe's method, or in terms of the haemoglobin content or red cell count, (82). Among those who believe that anaemia is of importance are Whittington and Miller (83), Marloff quoted by Morriss (84), Benyai and Anderson (85), Parenti (86) and Robins (81). The latter states that "the consensus of opinion is that anaemia increases and polycythaemia decreases the blood sedimentation rate and that in vitro experiments bear this out." Many other workers hold a similar view, but as recently as 1938, Cutler (87) showed that when corrections were made for anaemia, there was less conformity in the results so obtained. De Cecio and Elwood (88) gained a similar impression from their work. Day (80) showed in 1939, that no correction was necessary for diminished cell volume

in/

in the milder anaemias in the calculation of his sedimentin index. In 1921, Westergren (73) stated that the disturbing influence of variations in the red blood cells is, in phthisis, far less than might be expected. The most important factor seems to be that erythrocytosis of over five and a half millions at times can cause somewhat too low a figure. He pointed out that this might be of practical importance in dealing with patients treated by artificial pneumothorax. Previously (76), he stated that "from his reading of the literature and from his own calculations the opinion is gathered that in pulmonary tuberculosis normal or slightly raised red blood cell counts are found with surprising regularity."

Group 1.

(b) Plasma Proteins.

As noted previously in the short historical review, it had been observed by the end of the nineteenth century that agglutination of the red blood cells, caused by some change in the blood plasma, produced an increased sedimentation rate with the resulting appearance of buffy coat. Since then, the part which the plasma proteins play in the behaviour of sedimenting blood has been extensively studied.

Fahraeus/

Fahraeus (74) confirmed the fact observed by some of the nineteenth century workers, e.g. Scudamore, that the most important change in the blood plasma of persons with an increased sedimentation rate was an increase in its fibrinogen content. He showed too that the factor which Nasse had been unable to determine, was that an increase in serum globulin could also produce an increase in the sedimentation rate. He was also instrumental in elucidating the method by which these protein substances acted, and he showed that increased agglutination of the red blood cells, which is of great importance in increasing their sedimentation velocity, could be attributed to these protein fractions. In his experiments, he found that there was no agreement between the sedimentation velocity of the red corpuscles and the total plasma protein percentage, but, by fractional precipitation of the component proteins by ammonium sulphate, he observed that the sedimentation velocity of the corpuscles was greater in a solution of fibrinogen than in one of globulin, and greater in one of globulin than in one of albumin. He noted that a high sedimentation velocity of the corpuscles in plasma was generally accompanied by a similar sedimentation velocity in serum derived from the same blood. This he explained by the fact that in various pathological states/

states the plasma fibrinogen and the serum globulin show often a coincidental increase. This had previously been emphasised by Halliburton whom Fahraeus quotes. Levinson (89), like Fahraeus and many other workers, noted an increase in the plasma fibrinogen in pulmonary tuberculosis and, in his article, he quotes Frisch, who observed that the breaking down of tissue results in the liberation of enzymes which play an important role in the formation of fibrin. He quotes also Foster and Whipple, who showed that tissue injury and inflammation stimulate fibrinogen production, and Mills, who found that the lungs yield the most potent product which is capable of activating fibrinogen formation. In view of these facts, it is easily understood why the sedimentation rate is so often increased in pulmonary tuberculosis, especially in active and far advanced types of the disease. Levinson remarked also that in pulmonary tuberculosis there may be a reversal of the albumin-globulin ratio of these plasma proteins, the globulin fraction being markedly increased. This, too, leads to an increased sedimentation velocity of the red blood cells. In typhus, an increase in globulin percentage, without an increase in fibrinogen percentage, had been noted previously by Fahraeus (74) to coincide with an increased sedimentation velocity. He remarked, however, that too close a parallelism between the sedimentation rate and

the/

the globulin and/or fibrinogen increase should not be expected, as the total proteins do exert some influence also.

It is of interest to enquire why the increase in these protein fractions should produce an acceleration of the sedimentation rate. Fahraeus studied this aspect of the subject carefully, and, by his experiments, showed that the increase in sedimentation rate of the red blood cells is closely related to the viscosity of the solution in which they are suspended. As serum globulin and fibrinogen increase, the viscosity and hence the agglutinability of the red corpuscles increase,and so a physical basis for the phenomenon was partially established. Fahraeus emphasised also the part played by surface tension and the electric charge which the corpuscles possessed, but he seemed to believe that a physico-mechanical theory emphasising viscosity was most important. Fibrinogen and globulin solutions diminish the electrical charge of the red blood cells and so permit of the corpuscles adhering to each other more easily. In 1925, Fischel (90) stated that the modern school regard this latter phenomenon as being of importance,and he also remarked that the suspension stability of the red cells is a complex phenomenon which cannot be explained by one

theory/

theory.

It is opportune to comment briefly now on the physical factors involved in sedimenting blood. When blood which has been prevented from coagulating is set up in a vertical graduated tube, the red cells are seen to sediment at varying speeds in the blood of different individuals. When readings are taken at intervals of five minutes or longer, it is immediately seen that the rate of sedimentation varies considerably during the period taken by the process to reach completion. At first, there is a period of slow sedimentation, next,a period when the maximum velocity of sedimentation is attained, and finally, another period of slow sedimentation. During the first period, the red cells, in addition to beginning to sediment, undergo rouleaux formation thus producing corpuscular aggregates which sediment more rapidly as they increase in size. Stokes' law applies to the sedimenting particles. It states that "other things being constant, the rate of sedimentation is proportional to the square of the radius of the particle," (80). Day (80) believes that it is safe to assume that agglutination is complete when the phase of maximum sedimentation is reached. At this time the corpuscular aggregates have reached a definite size, either by the

rouleaux/

rouleaux joining together, or by the addition of individual corpuscles to the separate rouleaux. They sediment through the plasma at a constant velocity till packing begins, when the sedimentation readings again show a phase of slow sedimentation.

As the red blood cell aggregates fall, they are acted upon by several forces. Gravity causes them to descend, whereas the hydrostatic upthrust of the fluid in which they are suspended and also its viscosity, tend to counteract the effect of gravity. When these forces balance, and when the corpuscular aggregates have reached their maximum size, they fall through the plasma at a constant velocity till packing begins, (80). This constant velocity obeys Stokes' law which, expressed as an equation, is

$$\text{Velocity} = \frac{2}{9} g \frac{\text{density of the particle} - \text{density of the fluid}}{\text{viscosity of the fluid}} \times (\text{Radius of the particle})^2.$$

For the law to be obeyed, the fluid column should be of infinite extension, but it has been found by Schuster (91) and other workers, that if the internal diameter of the tube used to contain the fluid is greater than 2 mm., the results obtained in tubes of varying diameter are almost identical. In addition, the tube should

be/

be of sufficient length to allow of the maximum velocity being attained before packing occurs. In practice, the 200 mm. Westergren tube is sufficient to avoid errors. Day (80) finds that the phase of maximum velocity of sedimentation bears an exponential relationship to the amount of agglutinating substances in the plasma. For convenience, he refers to these substances as sedimentin and he proposes to express their effects by what he calls the "sedimentin index." He points out that it might be possible to calculate this index, by allowing a drop of citrated blood to stand for one hour in a specially devised counting chamber and counting the number of agglutinated clumps of cells at the end of that time.

The third phase in sedimentation, the phase of packing of the cells is of no great clinical importance. Actually, packing of the cells takes place at the beginning of sedimentation and progressively increases as time passes. A twenty-four hour reading of any sedimentation test is of no value beyond indicating cell volume.

Group 1.

(c) Factors of subsidiary importance.

1. White blood cells.

Robins/

Robins (81) quotes Von Varga who noted a close parallelism between total white cell count, the percentage of young leucocytes, and the speed of sedimentation. Ernstene (92) has noted a similar tendency. Cherry (93) could find no such relationship however.

2. The Blood Sugar Level.

An elevated blood sugar level may accelerate the sedimentation rate, but when the blood sugar is within normal limits its influence on the sedimentation rate is insignificant. This has been found to be so by Cherry (93). Robins' (81) survey of the literature showed that there was no definite agreement between the sedimentation rate and the concentration of cholesterol and lecithin in the blood. Fahraeus (74) showed that high concentrations of sodium chloride experimentally inhibit the sedimentation of the red blood cells, increasing their stability.

In the clinical study undertaken by the writer, the influence of these subsidiary factors has been studied specifically only in the relationship between the sedimentation rate and the white cell count. No patient investigated had diabetes.

Group 2.

(a) Age.

Fahraeus/

Fahraeus (74) noted that the suspension stability of the red cells was greatest in the new-born, a time at which the globulin fraction of the plasma proteins is also diminished. Ellensberg (94) has confirmed the low sedimentation velocity found in the new-born. In old age the sedimentation rate is increased, according to Lasch, whom Robins (81) quotes. The ages of the patients investigated ranged between 14½ and 50 years, but most fell between 15 and 30 years.

Group 2.
(b) Sex.

It has been noted by many investigators that the sedimentation rate is higher in the female. This fact Fahraeus (74) thought to be associated with the higher globulin values found in the female than in the male. In the writer's series of fifty patients, twelve were male and thirty-eight female.

Group 2.
(c) Menstruation.

Whitby and Britton (82) advise that blood should not be collected for the estimation of the sedimentation rate during the menstrual flow and also for a few days before and after it. Most workers corroborate this finding. In the writer's series a note of each menstrual period was taken and so due allowance could be made for any variation in the sedimentation rate at this time.

Group 2/

Group 2.

(e) Exercise.

Lockett (95) showed that after exercising normal medical students, the erythrocyte sedimentation rate increased. In some subjects its value was doubled compared with that noted before exercise. Some of the estimations performed by the writer were made in patients having come to the hospital after discharge, for the purpose of checking their progress. The exercise involved in this cannot be considered as severe, the patient being able to get transport to the hospital gate. The in-patients were generally at rest in the morning, at which time their blood was taken.

Group 2.

(f) The ingestion of food.

Lockett (95) found that the sedimentation rate was decreased during digestion, the maximum decrease occurring one to one and a half hours after a meal. In the writer's series the blood was withdrawn as near noon as was possible. This was four hours after the patient's last meal.

Accordingly, exercise and the ingestion of food were not of great importance in this investigation. Robins (81) quotes Von Varga and Rourke as stating that the time of day, the relationship to the ingestion of food/

food, and exercise, do not affect the erythrocyte sedimentation rate. Banyai and Anderson (85) have also stated that "they found the so-called physiological variations during a day or from day to day had no significance concerning the results or interpretation of the test."

Group 2.

(g) Drugs.

In an editorial note in "Clinical Excerpts" (96), it is said that the drugs which affect the erythrocyte sedimentation rate include morphia, aspirin, potassium iodide, asphenamine, and certain of the sulphonamides especially sulphapyridine. None of the patients in this series were receiving any of these drugs except perhaps aspirin occasionally. It may be noted here that smoking is said to affect the erythrocyte sedimentation rate according to Scoz and Faravelli. Their findings are quoted in an abstract in the journal "Tubercle." (97) .

Group 2.

(h) Barometric pressure.

Faravelli and Scoz, quoted again in an abstract in "Tubercle" (98), have stated that the lower the barometric pressure, the slower is the sedimentation rate/

rate. This factor is not of any particular importance in the writer's investigations as all the patients were subject to the same climatic conditions.

It is necessary to consider a third group of factors affecting the sedimentation rate. This group consists of the details of the technique employed.

1. The Anti-coagulant.

The writer used 3.8% sodium citrate solution as an anti-coagulant. Robins (81) quotes Walton as stating that citrate may slow the sedimentation rate. Sodium citrate has been widely used by various workers and no special investigation was made here into its property of retarding the sedimentation rate.

2. Room temperature.

Wintrobe and Landsberg (99) found that at room temperatures ranging between 19° and 23° C, there is no alteration in the sedimentation rate. The writer did not take room temperature readings. At higher room temperatures Fahraeus (100) has noted changes in the sedimentation rate which depend on alterations in the plasma proteins. Della Vida (101) states that the temperature variations in an ordinary laboratory are not likely to be of importance and Houghton (102) is of a similar opinion.

3. The tube.

The/

The Westergren 200 m.m. tube of internal diameter equal to 2.5mm. was employed in this investigation. This is considered satisfactory by most workers. Care was taken that the tubes were vertical in their stand, as tilting of the tubes is known to produce false readings. Walton (103) gives some estimate of the degree of the error which can be so produced.

4. The time interval between withdrawal of blood and beginning the estimation.

Della Vida (101) has shown that there is little change in the rate of sedimentation providing that the blood is set up for the estimation within five hours of its withdrawal. Thereafter, there is a progressive reduction in the sedimentation velocity. Day (80) has shown that the corpuscles after five hours lose their power of agglutinating; the plasma, however, retains its agglutinating influence, and using fresh washed corpuscles with 24 hour old plasma it is possible thus to estimate the sedimentation rate of the original specimen. All sedimentation tests in the writer's investigation were set up usually within two hours of withdrawal of the blood and the first hour reading was taken.

5. Venous stasis.

Banyai and Anderson (85) state that venous

stasis/

stasis will increase the sedimentation rate and Whitby and Britton (82) recommend only a light tourniquet when blood is being withdrawn. In practice, the writer followed their advice.

Having considered the factors which influence the erythrocyte sedimentation rate, it is opportune to mention the value which may be attached to this test in the diagnosis, treatment and prognosis of patients suffering from pulmonary tuberculosis.

It is generally recognised that in diagnosis the value of the test is minimal. Among those who corroborate this finding may be mentioned Rest (75), Wingfield (104) and Dunlop (105). There is some disagreement as to whether the erythrocyte sedimentation rate can give normal values in patients suffering from active disease. Westergren (73) found that the test did not give a normal value in patients with active or probably active tuberculosis. Clegg (106) found the test to be an accurate measure of the activity of the pulmonary lesion. On the other hand, Banyai and Anderson (85) found that 7.35% of two thousand patients with active pulmonary tuberculosis had a normal blood sedimentation rate. Houston, Harkness and Whittington (107) found on analysing the results of six hundred and fifty combined erythrocyte sedimentation rate and

plasma/

plasma viscosity measurements, that any simple and reliable correlation of the erythrocyte sedimentation rate with the pathological changes present in the body was not possible. McIntosh and Keay (108) state that "in the male subject the test may be of limited value although the information required by the physician in assessing a case can generally be obtained more accurately without its use. Since in the female subject the test carries an error of anything from 12 to 30%, its employment is, for practical purposes, valueless." They quote six series of patients, having active tuberculosis, examined by various workers. The percentages of these patients having abnormal erythrocyte sedimentation rates varied from 15 to 77%. It is therefore not surprising that they attach so little value to this test. Although the value of the test is very limited in assisting diagnosis, its value in following the progress of patients suffering from tuberculosis is somewhat greater. Davies (109) found the erthrocyte sedimentation rate to be an excellent guide to therapeutic measures. He quotes Tegtmeier as stating that a change in the blood sedimentation rate may precede a clinical change for the worse by six to eight days. The writer was especially interested in discovering whether this observation would be repeated

in/

in his series of patients who developed pleural effusions during artificial pneumothorax therapy. Banyai and Anderson (85) found also that the greatest merit of the test was in following the course of the disease and in assessing the results of treatment. Lewis-Fanning and Myers (110) found that the test did not supply any information that could not be derived from clinical examination and the study of routine radiographs, and they concluded that the value of the test did not justify the time and work spent in carrying it out.

In prognosis, the value of the test is thought by some workers to be considerable. Heaf (111) found that in eighty per cent. of patients, the prognosis might be correctly foretold by analysing the types of blood sedimentation rate curves found on admission to hospital. Penman (112) quotes the unpublished work of Lynn and Brooks. The former found that the prognosis in patients with a fluctuating blood sedimentation rate was almost as bad as that in patients having a rapid rate, while the latter found the prognosis to be good in patients discharged from the sanatorium with a series of consecutive monthly readings within normal limits. Davies (109) found the test to have its greatest value in prognosis.

Rest/

Rest(75),however,thinks that the value of the test in prognosis is not significant. Blanco and Fernandez (113) believe it cannot be relied on solely when assessing prognosis. De Cecio and Elwood (88) find that there is a great diversity of opinion as to the value of the test in this connection.

In spite of the disagreement in the observations of various workers, it was thought that this test, taken in conjunction with a total and differential count of the white blood cells, might be of value in the present investigation.

The Blood Picture.

Many investigations have been made during the treatment of phthisis patients by all the modern methods employed in sanatoria, and the results in many instances have not justified the time spent on examining serial blood films. Stobie, England and McMenemy (114), reporting a series of nine hundred and forty-seven blood examinations performed on phthisis patients, state that " although the sedimentation rate has a compliance with the clinical disease in the majority of instances, the additional information given by the laborious serial leucocyte counts does not justify their performance as a routine." They believe that little reliance can be placed on

haemograms/

haemograms in estimating the extent or following the progress of the disease. Elwood and De Cecio (88) state that "their results and conclusions support the seldom reported but not uncommon opinion of the clinical inadequacy and not infrequent fallibility of the white blood cell picture." Other workers do not take such a pessimistic view; they include Houghton (115), Morriss and Wilson (116) who found a seventy-five per cent. agreement between haemograms and the clinical picture, Deegan (117) and Medlar and Pesquera (118). Elwood and De Cecio (88) report some instances in which serial counts could have been of value in anticipating events, and this observation was constantly before the writer when performing blood tests. Before proceeding to a consideration of the findings obtained in this investigation, a review of the literature on the individual items of the haemogram will be presented.

1. <u>The Total White Blood Cell Count</u>.

Normally, there is a considerable range within which the total leucocyte count fluctuates. Wright (6) gives the range as 5,000 to 10,000 cells per cubic millimetre with an average of 6,000 to 8,000 per c.mm. as/

as normal. He states that considerable variations between these limits may occur in the same individual from day to day or even from hour to hour. Whitby and Britton (82) give the normal range of the white blood cell count as 4,000 to 11,000 per c.mm. This being so, it would seem unwise to attach very much importance to fluctuations of the leucocyte count within these values when dealing with tuberculous patients. Stobie, England and McMenemy (114) mention this point of view in their article. They state that as tuberculous disease advances the total white blood cell count rises.

The normal range of the total leucocyte count is dependent on various factors. Shaw (119) has shown that there occur two leucocyte tides each occupying twelve hours during a day. There is a variation of two thousand or more in the total white blood cells per cubic millimetre and this variation affects mainly the neutrophils. It occurs regardless of food or exercise. Wright (6) states that the leucocytosis said to occur after meals probably represents normal random fluctuations in the white blood cell count. Adelman (120) could find no post-prandial leucocytosis in his investigations.

Whitby/

Whitby and Britton (82), quoting Ahlborg, state that there is a small increase in the leucocytes one hour after a protein meal, that this increase is maximal in four hours and subsides in six hours. The total seldom exceeds 11,000 leucocytes per cmm. The afternoon rise in the total white blood cell count may be related to this post-prandial rise. Exercise, physical or mental, emotion and exposure to ultra-violet rays all cause an important increase in the leucocytes, (82). Kaminsky (121) recommends performing leucocyte counts under basal conditions, for he found considerable variations in the leucocyte count, total and differential, after exercise. Medlar (122) has observed variations of 2,000 to 4,000 cells per cmm. in the total leucocyte count whether the subject was at rest or working. The majority of blood examinations performed by the writer were done with the patients at rest and three to four hours after a meal.

When an individual develops tuberculosis, it is found that the total white blood cell count tends to rise. Duffy (123) found that a moderate leucocytosis occurred frequently in patients with moderately advanced and far advanced disease. Patients with minimal disease sometimes showed a slight leucocytosis. Medlar (122) believes that the total white/

white blood cell count roughly reflects the volume of deranged tissue with which the leucocytes have to cope, but qualifies this by saying that the extent or location of the tuberculous process cannot be told by the leucocyte reaction, for an incipient case may show as abnormal a count as a far advanced one. Stobie, England and McMenemy (114) found that as tuberculous disease advances in the lungs, the white blood count rises due to an absolute neutrophil leucocytosis. Kelley (124), Boissevain, Forster and Good (125), and Elwood and De Cecio (126) agree with this finding. Sweaney (127) found the total white blood count to be very variable. Houghton (102) states that he no longer uses the total white blood count as it does not greatly increase the information derived from the differential count. Medlar (128) found that exercise lowered the total white blood count in five tuberculous patients with moderately advanced disease, but that this also occurred in six non-tuberculous patients. Considering the variations which may occur in the total leucocyte count due to physiological or pathological processes, it will not be surprising if it fails to assist greatly in the writer's investigations.

2. <u>The Differential White Blood Cell Count</u>.

There is a considerable variation in the figures given for the normal percentages of the various cells by different workers. Frimodt-Möller and Barton (129) found the average neutrophil percentage in seventy-five normal persons to be forty-seven. In their article, they give the percentages thought to be normal by other workers. These are as follows:-

1.	Ehrlich	70-72%.
2.	Stitt	65%.
3.	Medlar	65% (upper limit of normal).
4.	Oatway	50-65%
5.	von Bonsdorff	45.9%

Frimodt-Möller and Barton (129) examined also twenty-four tuberculous patients who were well and working, and thirty-eight non-tuberculous patients who had no disease. They found the average neutrophil percentage to be 48% and 51.5% respectively for these groups. They therefore give what they consider to be the normal range of the neutrophil percentage as 45-55%. Whitby and Britton (82), quoting Osgood et al., give the neutrophil percentage as ranging from 33-75%. Furthermore, they state that according to Sabin, Cunningham, Doan and Kindwall, "there is a rhythmical fluctuation of the polymorphonuclear leucocytes every hour, that the highest count in any individual may be twice as much as

the lowest, and that the highest count occurs between 1 p.m. and 5 p.m." Garrey and Bryan, quoted by Wright (6), give 70% as the normal neutrophil percentage, the range being 60-70%. It would seem wise to adopt as normal Oatway's figures of 50-65% as being well within the extreme limits quoted by other workers.

Garrey and Bryan (130) state that studies during exercise reveal an increase in the total leucocytes and an increase in the neutrophils. Medlar (128), however, found that in non-tuberculous persons the ratio of neutrophils to lymphocytes was reduced by exercise, but that in tuberculous patients the ratio increased slightly. The immediate effect of exercise on the average percentage of neutrophils and lymphocytes in non-tuberculous persons was nil, whereas with tuberculous patients there occurred a slight drop in the lymphocytes and a slight rise in the neutrophils. However, the final result was a drop in the neutrophil percentage and a rise in the lymphocyte percentage of the non-tuberculous group, and a much smaller drop in the neutrophil percentage and also a drop in the lymphocyte percentage of the tuberculous group. These effects did not occur in every individual investigated, and Medlar (128) believes that the change, or lack of it, in the leucocyte picture during exercise, merely reflects/

reflects the effect produced on the pathological process. These changes are important in the treatment of patients by graduated exercise, and should a pleural effusion occur in an ambulant patient treated by artificial pneumothorax, the effect of exercise on the haemogram, as well as the effect of the complication, will have to be considered.

The leucocytosis which follows a meal need not be considered here, for the writer's patients had no meal during a period of three to four hours before the withdrawal of blood.

Boissevain and Chapman (131) found that a rise in altitude from sea level to 6,000 ft. caused a fall in the neutrophil count from 60.8% to 52.4%. These were the average figures found in different groups of patients in two sanatoria situated at the levels mentioned. Robroyston Sanatorium is situated 350 feet above sea level. Any effect on the neutrophil percentage falls well within the limits of normal as given by Oatway.

Stobie, England and McMemeny (114) believe that more accurate differential white cell counts can be made by preparing films by the coverslip method than by using the slide method. The former method is accompanied by less trauma to the cells and drying

is/

is quicker. Heaf (132) found great variations in the counts performed by eleven different authorities on films made at the same time from a freely flowing stab wound in the ear of three different patients. The neutrophil percentage varied from 38% to 72% in the first patient, 59% to 76.5% in the second patient and 30.5% to 51% in the third patient. This discrepancy was considerably reduced by using venous blood to make the films. An excess in monocytes in blood withdrawn from the ear was a source of error which may have been responsible for some of the wide variations noted in the first counts. Schilling (133) noted that monocytes seem to stagnate in the ear vessels in normal people.

It is obvious, then, that there are many limitations to the value which can be attached to a differential leucocyte count. The variations seen in the neutrophil count occur also in the other cells to be considered. So far as tuberculosis is concerned, it has been pointed out by Houghton (102) that in the interpretation of a differential leucocyte count, there are three key cells to consider:- neutrophils, lymphocytes and monocytes. Medlar and Kastlin (134) state that in different phases of development of tuberculous lesions there is a quantitative and qualitative difference in their cellular content. This they regard as being due possibly to a chemical change in the tissues composing the/

the lesion. Medlar (135) believes that the mononuclear cells play the chief role in the formation of the primary tubercle. If healing should occur at this stage, the inflammatory exudate is resorbed and lymphocytes infiltrate the lesion. If, however, the mononuclear cells are unable to combat the invasion of tubercle bacilli, then neutrophils are attracted to the lesion. If these cells live, suppuration and cavity formation may occur. If they are killed and their proteolytic enzyme ceases to function, then caseation occurs. The lesion is next invaded by monocytes and lymphocytes, and gradual encapsulation of the caseous material ensues. It may be that the caseous material is not all removed by absorption and organisation, and, should it persist, it will in some instances become calcified. The leucocyte response should give some information as to the predominant phase of the tuberculous process, but Medlar and Kastlin (134) point out that such a response cannot be measured in the circulating blood until the extent of the damaged tissue is sufficient to call out an abnormal number of cells of any type. The large variation in the stages of development of separate lesions in any one individual, means that the differential leucocyte count must be interpreted on general lines and be supplemented by clinical and radiological findings. Medlar and Pesquera (118) state that "the monocyte represents/

represents tubercle formation, the neutrophil represents the tubercle undergoing abscess formation, and the lymphocyte represents the healing phase of the tuberculous lesion." In the diagnosis, prognosis and treatment of tuberculosis, different workers accord varying values to the individual items of the differential count. Some stress the neutrophil percentage or absolute number, and others the lymphocyte/monocyte ratio. Thus, Boissevain and Chapman (131) found that there was a definite correlation between the neutrophil percentage and the outcome of the disease. They found, also, that the monocytes sometimes showed a similarly high correlation, but that the lymphocytes lacked any correlation with the subsequent condition of the patient. Boissevain, Forster and Good (125) advance similar findings, and so also do Elwood and De Cecio (126). On the other hand, Cunningham, Sabin, Sugiyama and Kindwall (136) found that the course of a tuberculous lesion could be accurately followed by noting the relative proportions of monocytes and lymphocytes in the blood of rabbits. Morris and Tan (137) found in tuberculous patients that the lymphocyte/monocyte ratio offered an extremely useful means of estimating the patient's reaction to the tubercle bacillus. They give a lymphocyte/monocyte ratio of 3/1 as the line of demarcation between a normal and an abnormally low ratio/

ratio. Their patients with active pulmonary tuberculosis had an average lymphocyte/monocyte ratio of 2.52/1, while for the inactive group of patients the figure was 4.5/1. A non-tubercular group they found to have an average ratio of 5.45/1.

So far as the eosinophil and basophil cells are concerned, Medlar and Kastlin (134) state that "they may be increased or decreased in cases showing the worst type of leucocyte picture, or in cases which show the least variation from the normal formula." They therefore do not attach any diagnostic or prognostic value to these cells. Houghton (102), however, believes that the eosinophil cells are an asset to the patient in his reaction to tuberculous disease, for in his index he links them together with the lymphocytes. The range of possible values for Houghton's index is from zero to three hundred, the higher the value the better being the condition of the patient. In the calculation of the index, lymphocyte and eosinophil percentages are doubled, for these cells are considered in relation to both neutrophils and monocytes. Other indices such as the Frimodt-Möller and Barton Index, Crawford's Index and Medlar's index are in use.

It is opportune to mention here the

significance/

significance of the von Bonsdorff count. In 1904, Arneth (138) divided the neutrophil polymorphs into five classes according to the shape and number of divisions in the nucleus. He subdivided these classes making the count very complicated. Von Bonsdorff (139) later simplified the count, and Cooke (140) set forth a simple and practical method of performing a nuclear count. Class I cells have an individual nucleus, and classes II to V have the nucleus divided and the portions of it separated by fine chromatin bands varying in number from one to four. Class II has one chromatin filament, class III, two filaments, and so on. The normal figures for the various classes are, class I 10%, II 25%, III 47%, IV 16%, V 2%. By multiplying the percentage of cells in each class by the class number and adding these figures together we get the number 275. This is considered to be the normal figure for the von Bonsdorff count.

Houghton (115) thinks that this figure is somewhat high, and after having investigated over one thousand patients with pulmonary tuberculosis, he found that there were very few whose von Bonsdorff count did not show a left shift, or lowering of the count, even after completion of their treatment. Paine and Austin (141), using a modification of this count, the

filament-nonfilament count as they term it, found that it reflected the amount and degree of activity of the disease. They found it to be superior to Crawford's index. Duffy (123) found the Schilling method of classifying the neutrophil leucocytes to be of some value in the detection of clinical relapses. Left shifting of the Schilling count occurred in some patients before there were any other symptoms or signs of a relapse. Unfortunately, however, left shifting was not always followed by a relapse, so reducing the value of the Schilling count considerably. Duffy (123) found that in estimating activity in pulmonary tuberculosis, the order of appearance of the clinical findings was often leucocytic reactions, erythrocyte sedimentation rate, X-ray shadows, and lastly, signs and symptoms. This, however, was not invariable. Briskman (142) found that the Schilling count seemed to reflect the progressive and more acute processes of tuberculosis, whereas the latent chronic infections were better expressed in the erythrocyte sedimentation rate.

The short review given above of the total and differential leucocyte counts will, it is hoped, serve to show some of the difficulties which are encountered in the interpretation of haemograms in tuberculous infection. Medlar and Kastlin (134) state

that "a majority of authors have concluded that a study of the leucocytes reveals nothing of diagnostic or prognostic value. A few authors believe it to be of value and urge its use along with other methods as a helpful guide in the care of the tuberculous."

Observations.

As noted previously, twenty-five of fifty patients on whom serial blood counts were performed, developed a pleural effusion. It was found that the more advanced and the more acute was the disease, the more likely was an effusion to occur. The writer was anxious to know if the initial blood picture bore a similar relation to the disease, and whether there was a significant difference in the blood picture of those who developed an effusion and those who did not do so.

The following table is a composite one drawn up from the average figure found by a consideration of many individual readings.

Table 28. Mean values of initial blood findings.

Clinical Classification.	Moderately Advanced.		Far Advanced.									
			I.		II.		III.		IV.		V.	
Data.	N.E.	E.	N.E.	E.	N.E.	E	N.E.	E	N.E.	E.	N.E.	E.
Total white blood cells/cmm.	10,000.	11,100.	8,266.	-.	5,400.	9,200.	15,566.	11,933	10,460.	12,155	16.000	11,100.
Neutrophil %.	60.3.	53.8.	58.6.	-.	53.5.	64.6.	69.4.	57.6.	61.5.	63.8.	61.5.	70.5.
Eosinophil %.	2.	2.4.	3.1.	-.	0.5.	1.9.	1.	2.3.	5.	2.4.	2.	3.
Basophil %.	0.5.	0.6.	0.3.	-.	0.	0.7.	0.16.	0.3.	0.1.	0.5.	1.	0.75.
Small Lymphocyte %.	28.5.	29.7.	28.	-.	30.5.	17.3.	17.6.	25.3.	23.7.	19.4.	11.5.	19.25.
Large Lymphocyte %.	4.	5.4.	4.	-.	5.5.	4.9.	2.5.	5.8.	3.7.	4.2.	11.	1.5.
Monocyte %.	8.2.	8.	6.	-.	10.	10.7.	9.2.	7.5.	6.2.	10.1.	13.	5.
Lymphocyte/ Monocyte ratio.	4.8/1.	4.8/1.	5.7/1.	-.	3.6/1.	2.3/1.	2.2/1.	4.1/1.	4.2/1.	2.9/1.	2.2/1.	4.4/1.
Von Bonsdorff Count.	230.	206.	223.	-.	174.	201.	216.	183.	229.	197.	143.	210.
Erythrocyte Sedimentation Rate at 1 hour.	23.	16.	12.	-.	70.	53.	47.	15.	18.	52.	19.	21.
Houghton's Index.	205.	207.	216.	-.	113.	122.	135.	167.	185.	129.	99.	157.
Number of Patients.	9.	6.	3.	0.	1.	5.	6.	3.	5.	9.	1.	2.

N.E. = Non-effusion Group.

E. = Effusion Group.

As the extent of tuberculous involvement of the lungs increases according to the classification used, the changes in the haemogram are as follows:-

1. Total White Blood Cells.

There is an increasing tendency towards a leucocytosis as the disease advances, but this is by no means constant. Those patients who later develop effusions do not necessarily have a higher white cell count at the initial reading than those who do not develop effusions.

2. The Differential Count.

The neutrophil percentage does not constantly increase as the disease advances in this series of patients, and no weight can be attached to this count in assessing the possibility of an effusion developing. The lymphocyte percentage tends to fall as the disease advances, and again,no indication is given by this count as to the possible complication of an effusion. The monocyte percentage is generally elevated in all the groups, but there is no remarkable difference between the figures given for the effusion and non-effusion groups, except in sub-group V of the far advanced patients. Eosinophil and basophil percentages are not of significant value.

3./

3. The Lymphocyte/Monocyte ratio.

This is an extremely variable figure and offers no help in differentiating the two groups.

4. Von Bonsdorff Count.

This figure tends to fall as the disease advances but this finding is not constantly noted. The effusion group of patients sometimes have a lower count than the non-effusion group, but this too is not by any means invariable. The normal von Bonsdorff reading is 275 and, on the whole, the average readings are low.

5. Erythrocyte Sedimentation Rate.

The results are variable and no significance can be attached to the initial erythrocyte sedimentation rate as a prognostic index of the possibility of an effusion occurring.

6. Houghton's Index.

Houghton (115) gives 260 as a normal figure for his index. The index tends to fall as the disease advances but this is not invariable. It offers no help in differentiating the effusion and non-effusion groups.

Comment/

Comment.

There is an increasing tendency to a leucocytosis with the production of younger neutrophil cells as pulmonary tuberculosis advances. The erythrocyte sedimentation rate and the lymphocyte/monocyte ratio are unreliable as indices of the extent of the disease. Houghton's index tends to fall as the disease advances, but in this series the extent of the fall is not proportional always to the extent of the disease. This is to be expected, for the erythrocyte sedimentation rate takes an important place in the index. These findings are in general agreement with those of Stobie, England and McMenemy (114), although the writer does not find the higher figures for the erythrocyte sedimentation rate occurring in the most advanced group. This may be due to the fact that only three of his patients fall into subgroup V of the classification. Houghton (102) believes the erythrocyte sedimentation rate to be an indicator of the disturbance in the patient's metabolism, and it may be that those three patients were, in fact, little upset generally by the disease. This, so far as could be judged clinically, was so in two patients, but the third (18, R.A.) was certainly acutely ill. Spector and Meuther (143) found that the erythrocyte sedimentation elevation and the left shift in the Arneth

Arneth count were directly proportional to the amount of involvement of the disease, and Masten (144) found that Medlar's index and the erythrocyte sedimentation rate reflected the extent of disease in the lungs. Frimodt-Möller and Barton (129) also found that the erythrocyte sedimentation rate, the neutrophil percentage and the Schilling count, all deteriorated as the disease advanced. Their observation that the lymphocyte percentage fell as the disease advanced is similar to the tendency noted in this series. The monocyte percentage remains remarkably stationary throughout the various groups in the writer's series. This fact had also been observed by Stobie, England and McMenemy (116), and it is for this reason that they believe the lymphocyte / monocyte ratio to be of little value; the small variations which occur are cancelled out by division of the factor . They too, found a falling lymphocyte percentage as the disease advanced.

The acuteness of the tuberculous process in the lungs is usually reflected in the clinical picture which the patient presents, and it is with this in mind that the next table is drawn up in a similar fashion to table 28. In it, the various blood findings are/

are charted against the symptom-group of the patient, for the two groups, non-effusion and effusion. The symbols A, B, and C are employed to denote the symptom-groups as outlined by The National Tuberculosis Association of America.

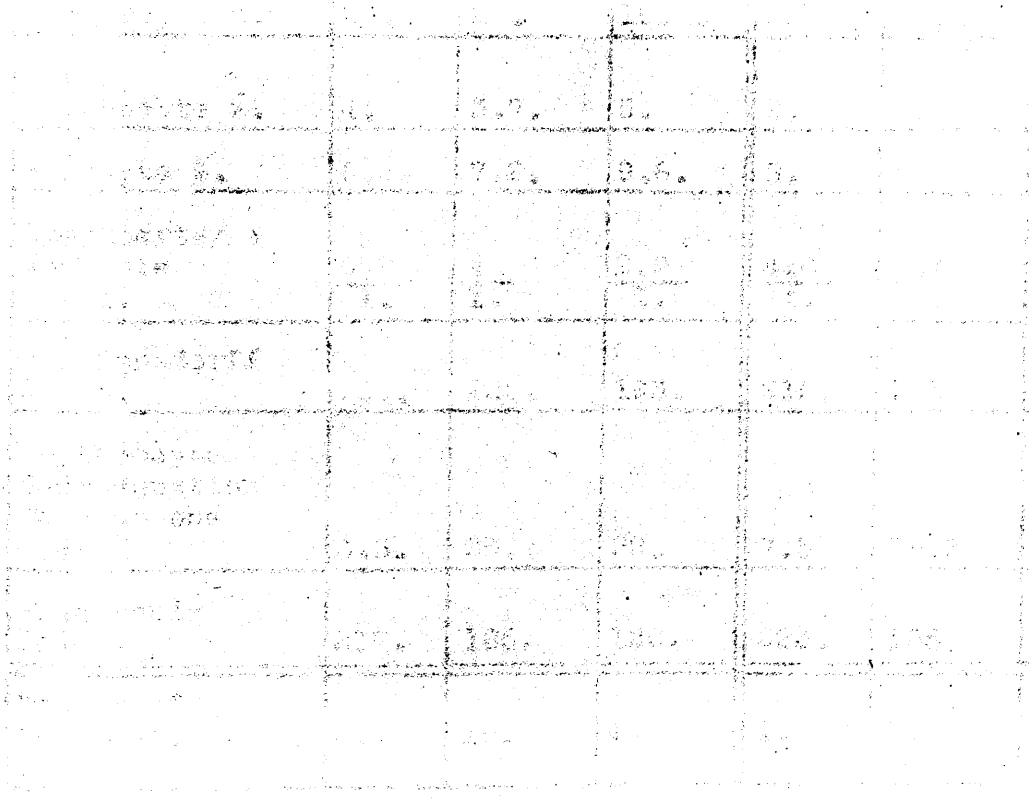


Table 29.

MEAN VALUES OF INITIAL READINGS IN RELATION TO SYMPTOM. GROUPING.

Data.	Non-effusion Group.			Effusion Group.		
	A.	B.	C.	A.	B.	C.
Total white blood cells/cmm.	9,400.	11,542.	10,950.	9,800.	11,542.	11,421.
Neutrophil %.	60.7.	62.2.	63.6.	53.5.	55.	64.2.
Eosinophil %.	1.7.	2.6.	1.9.	1.5.	2.1.	2.2.
Basophil %.	0.2.	0.3.	0.4.	0.	0.5.	0.6.
Small Lymphocyte %.	29.	25.	19.4.	35.	27.6.	19.
Large Lymphocyte %.	4.	3.7.	5.	2.	6.	3.6.
Monocyte %.	5.2.	7.2.	9.6.	8.	8.	9.4.
Lymphocyte/ Monocyte Ratio.	$\frac{6.2}{1.}$	$\frac{4}{1.}$	$\frac{2.9}{1.}$	$\frac{4.6}{1.}$	$\frac{4.4}{1.}$	$\frac{2.9.}{1.}$
Von Bonsdorff Count.	223.	225.	193.	215.	193.	201.
Erythrocyte Sedimentation Rate at one hour.	3.5.	26.	52.	7.5.	18.5.	46.
Houghton's Index.	217.	185.	120.	223.	185.	142.
Number of Patients.	2.	19.	4.	1.	7.	17.

The blood findings considered in relation to the symptom-grouping already described seem more significant than similar findings considered in relation to the stage of the pulmonary disease.

1. Total White Blood Cell Count.

There is a significant increase in the total white blood cell count in those patients with definite symptoms, i.e. groups B and C. This applies both to the non-effusion and effusion groups, but there is no significant difference between these groups.

2. The Differential Count and Lymphocyte/Monocyte Ratio.

The neutrophil percentage increases as the symptoms become more severe, but the effusion group usually shows a lower percentage than the non-effusion group. The eosinophil and basophil percentages are of no special significance. The lymphocyte percentage falls as the symptoms increase in severity, and the non-effusion group of patients shows a lower percentage usually than the effusion group. The monocyte percentage increases as the lymphocyte percentage falls, and there is remarkably little difference between the non-effusion and effusion groups. As one would expect from these findings, the lymphocyte/monocyte ratio falls also as the symptoms increase, and again there is no marked difference in the non-effusion and/

and effusion groups.

3. Von Bonsdorff Count.

This reading tends to fall as the symptoms increase, but this is not invariable and in general the effusion group has a lower value.

4. Erythrocyte Sedimentation Rate.

The erythrocyte sedimentation rate rises progressively from groups A to C, and it is higher in those patients who did not develop an effusion.

5. Houghton's Index.

Houghton's index falls as the symptoms become worse and usually the effusion group shows higher values than the non-effusion group.

Comment.

The haematological findings seem to be more closely related to the condition of the patients as judged by the signs and symptoms of toxaemia, rather than to the extent of the disease. As signs and symptoms of toxaemia reflect the acuteness of the disease, apart from those signs due to mechanical destruction of lung tissue and fibrosis, as manifested by circulatory embarrassment, it would appear, according to the writer's observations/

observations, that the haemogram gives an estimate of the severity but not necessarily of the extent of the lesion. Stobie, England and McMemeny (114) quote Medlar as stating that an incipient case of tuberculosis may show as abnormal a leucocyte count as one in which the disease is far advanced, and this tends to be borne out by the writer's findings, although, as previously observed, not a few workers found more evidence of deterioration in the haemogram as the disease advanced than is the case in this series.

The findings for those patients who developed an effusion and those who did not, are so variable, that they cannot be used in assessing which patient may later develop an effusion. This is not unexpected when the wide range of variation in the counts of individual patients within each group is considered. Clinically, it would have been of little value to have been able to foretell which patient would develop an effusion, for the pneumothorax would not have been abandoned on that score.

Stobie, England and McMenemy (114) quote Medlar and Pesquera and Deegan and Houghton as stating that "the haemogram is useful in following the progress of collapse therapy, pleural effusions not materially altering the picture." However, Houghton (102) himself states/

states that "acute pleurisy and acute pleural effusions depress all the features of the haemogram to an exaggerated extent." It was the writer's intention to discover what changes occur in the haemogram antecedent to and coincident with the development of an effusion, and if possible, to assess what change, if any, occurs in those patients who develop a tuberculous empyema as a sequel to a serous effusion. As before, tables are drawn up of the mean values of the various items in the haemogram. The antecedent findings are the readings noted up to fourteen days before the effusion is observed clinically or fluoroscopically, the coincident findings are those noted as soon as the effusion has appeared, and the delayed findings are those noted one to two weeks after the first occasion on which fluid has been observed.

It should be recognised that the relation between the blood picture and the onset of a pleural effusion in patients treated by artificial pneumothorax, may not always be easily determined. Many of these patients have markedly abnormal blood pictures and the onset of a complication may not alter this to any great extent. Hence, it is necessary to use some standard in determining the degree of change so far as this indicates a spread of the disease or deterioration in the patient's condition. The following scheme used in drawing up table 31 was adopted.

TABLE 30.

Data.	Change.		
	Minimal.	Moderate.	Maximal.
Total white blood cells.	Rise of 1000-3000 per cmm.	Rise of 3000-5000 per cmm.	Rise over 5000 per cmm.
Neutrophils.	Rise of 5%.	Rise of 5-15%.	Rise over 15%.
Lymphocyte/ Monocyte Ratio.	Fall of $\frac{0.5}{1}$ - $\frac{1}{1}$.	Fall of $\frac{1}{1}$ - $\frac{2}{1}$.	Fall over $\frac{2}{1}$.
Von Bonsdorff Count.	Fall of 5-15.	Fall of 15-30.	Fall over 30.
Erythrocyte Sedimentation Rate.	Rise of 10-15 mm.	Rise of 15-40 mm.	Rise over 40 mm.
Houghton's Index.	Fall of 5-20.	Fall of 20-50.	Fall over 50.

Another difficulty encountered is the determination of the exact time of development of an effusion. Clinically, this is not always easy, and many of the patients were too ill to stand fluoroscopic examination. In addition, when it is realised that the total number of blood examinations performed was one thousand and sixty-two, and that most of these were done/

done at fortnightly intervals, it is seen that had more frequent examinations been done, the number of patients examined would have had to have been reduced as the writer's routine hospital work had also to be done. For this reason it was thought best to retain the number of patients investigated at fifty, and to perform weekly blood counts only when there was a suspicion of fluid developing. In all, twenty-five patients developed an effusion. One of these effusions occurred a considerable time after the patient's discharge, by which time her blood examinations had been discontinued. Two other patients had a small puddle at the time of the first blood examination. These three patients were therefore not included in Table 31.

Comment on Findings.

A. Antecedent findings. 1. Total White Cell Count.

It is interesting to note that only in 31.5% of patients does the white blood cell count indicate that there may be a complication about to occur, and in the majority of these patients the change is minimal. In 40.5% the findings indicate an improvement and in 22.5% no change.

Table 31. Haemogram in Relation to the Onset of an Effusion.

	Total white blood cells.		Neutrophils.		Lymphocyte/ Monocyte Ratio		Von Bonsdorff Count.		Erythrocyte Sedimentation Rate.		Houghton's Index.	
	No.	%.	No.	%.	No.	%	No.	%.	No.	%	No.	%.
Antecedent Findings.												
No change.	5.	22.5.	7.	31.5.	2.	9.	2.	9.	6.	27.	1.	4.5.
Deterioration.												
Minimal.	4.	18.	1.	4.5.	2.	9.	2.	9.	3.	13.5.	7.	31.5.
Moderate.	2.	9.	7.	31.5.	6.	27.	3.	13.5.	7.	31.5.	7.	31.5.
Maximal.	1.	4.5.	1.	4.5.	3.	13.5.	2.	9.	1.	4.5.	2.	9.
Improvement.	9.	40.5.	5.	22.5.	8.	36.	12.	54.	4.	18.	4.	18.
Unknown.	1.	4.5.	1.	4.5.	1.	4.5.	1.	4.5.	1.	4.5.	1.	4.5.
Coincident Findings.												
No change.	1.	4.5.	8.	36.	3.	13.5.	3.	13.5.	2.	9.	0.	0.
Deterioration.												
Minimal.	3.	13.5.	1.	4.5.	2.	9.	4.	18.	3.	13.5.	2.	9.
Moderate.	5.	22.5.	5.	22.5.	7.	31.5.	2.	9.	10.	45.	6.	27.
Maximal.	3.	13.5.	1.	4.5.	5.	22.5.	6.	27.	5.	22.5.	11.	49.5.
Improvement.	10.	45.	7.	31.5.	5.	22.5.	7.	31.5.	2.	9.	3.	13.5.
Delayed Findings.												
No change.	2.	9.	4.	18.	2.	9.	0.	0.	4.	18.	1.	4.5.
Deterioration.												
Minimal.	6.	27.	0.	0.	4.	18.	4	18.	1.	4.5.	0.	0.
Moderate.	1.	4.5.	7.	31.5.	4.	18.	2.	9.	8.	36.	5.	22.5.
Maximal.	2.	9.	2.	9.	5.	22.5.	5.	22.5.	6.	27.	10.	45.
Improvement.	11.	49.5.	9.	40.5.	7.	31.5.	10.	45.	3.	13.5.	6.	27.

A. Antecedent findings. 2. Neutrophils.

In a somewhat higher percentage, 40.5%, the neutrophil count indicates a possible change, but in 22.5% it indicates an improvement, and in 31.5% no change. Its value is therefore not much greater than that of the white blood cell count. The change is a moderate one in the majority of patients.

A. Antecedent Findings. 3. Lymphocyte/Monocyte Ratio.

In 49.5% of patients the Lymphocyte/Monocyte Ratio indicates a deterioration, and again the change is moderate in a majority of patients. 36% show an improvement and 9% no change.

A. Antecedent Findings. 4. Von Bonsdorff Count.

In 31.5% of patients a deterioration is indicated, 54% show an improvement and 9% no change.

A. Antecedent Findings. 5. Erythrocyte Sedimentation Rate.

49.5% of patients show a deterioration and in 31.5% of this category the deterioration is moderate. 27% show no change and 18% show an improvement. As mentioned previously, menstruation may affect the sedimentation rate. In the writer's series of fifty patients, it was noted that only in six patients did menstruation appear to cause a rise in the sedimentation rate, and, as this increase was always less than 10 mm., it fell outwith the change considered as minimal. The possible effect is therefore not considered.

A/

A. Antecedent Findings. 6. Houghton's Index.

72% of patients show a deterioration, this being minimal and moderate in 31.5% of each respectively, and maximal in 9%. 18% show an improvement and 4.5% show no change.

The findings indicate that Houghton's Index is the most reliable factor in assessing the onset of a complication. The erythrocyte sedimentation rate and Lymphocyte/Monocyte Ratio are of less value, and the neutrophil percentage, the white blood cell count and the von Bonsdorff count are least reliable. It is interesting to note that in 40.5% of patients the white blood cell count falls prior to the onset of fluid. This does not amount to a leucopenia in any patient and therefore cannot be looked on as evidence of a severe toxaemia. It is thus classified under the section:- improvement. It may not, in fact, indicate an improvement, but rather the increasing toxaemia, evident clinically in several patients, may have caused a temporary fall in the output of new white blood cells. The improvement in the von Bonsdorff count in 54% of patients may have been due to a similar cause. Houghton (115) believes that clinical breakdown can often be anticipated by serial blood counts, but in his article no detailed analysis of findings for a group of patients developing a pleural effusion during artificial

pneumothorax/

pneumothorax therapy is given.

B. Coincident Findings. 1. Total White Cell Count.

In 49.5% of patients a deterioration occurs, and this is moderate in 22.5%, minimal in 13.5%, and maximal in 13.5% of that group. 45% of patients show an improvement and 4.5% no change. A rise in the percentage of patients showing a leucocytosis is therefore now evident and the change is becoming more marked. There is still, however, 45% of the patients showing a fall in this count.

B. Coincident Findings. 2. Neutrophils.

In 31.5% of patients an improvement and in a similar percentage, a deterioration is noted, while 36% show no change.

B. Coincident Findings. 3. Lymphocyte/Monocyte Ratio.

63% of patients show a deterioration, a majority of this percentage showing a moderate change. This is a 13% increase over the antecedent Lymphocyte/ Monocyte ratio. However, 13.5% show no change and 22.5% an improvement.

B. Coincident Findings. 4. Von Bonsdorff Count.

54% of patients show a deterioration and the majority of this group show a maximal change. This is again an increase of 22.5% over the antecedent Von Bonsdorff count for those showing a deterioration. 13.5%

show no/

no change and 31.5% an improvement.

B. Coincident Findings. 5. Erythrocyte Sedimentation Rate.

81% show a deterioration, a majority showing a moderate change. This is again a 31.5% increase over the antecedent findings for those showing a deteriorating value. 9% show no change and 9% show an improvement.

B. Coincident findings. 6. Houghton's Index.

85.5% show a deterioration, and in a majority this is maximal. 13.5% show an improvement. For those showing deterioration there is a 13% increase over the previous figure.

In short, all the findings apart from the neutrophil percentage indicate that there is a much higher percentage of patients showing deterioration in the haemogram coincident with the onset of an effusion than prior to it. In addition, the deterioration has become more marked, as evidenced by the greater percentage falling into the group showing a maximal deterioration. The clinical condition of a patient during the development of an effusion is usually such that a haemogram provides only corroborative evidence of the temporary deterioration which has appeared. Of the twenty-two patients included in this table, only two showed no gross clinical symptoms or signs of the onset of an effusion (13, G.McC., 40, M.M.). One showed a slight change in the blood findings as the effusion developed, while the other, who had bilateral

pulmonary/

pulmonary tuberculosis, showed little change at all. Thus, with those patients in whom it is difficult to detect fluid clinically, it is also difficult to do this by an examination of the blood.

C. Delayed Findings. 1. Total White Cell Count.

40.5% of patients show a deterioration in this estimation, i.e. fewer than the number showing a coincident deterioration but greater than the corresponding antecedent number. In most of these patients the deterioration is minimal. 9% show no change while 49.5% show an improvement.

C. Delayed Findings. 2. Neutrophils.

40.5% show a deterioration, i.e. the same percentage as the antecedent findings but higher than the coincident findings. 40.5% show an improvement and 18% no change.

C. Delayed Findings. 3. Lymphocyte/Monocyte Ratio.

58.5% of patients show a deterioration, 31.5% an improvement and 9% no change. Again, a higher percentage show a deterioration compared with the coincident findings.

C. Delayed Findings. 4. Von Bonsdorff Count.

49.5% show a deterioration and 45% an improvement. The percentage showing a deterioration is higher than that noted in the antecedent findings but lower than that noted in the coincident findings.

C/

C. Delayed Findings. 5. Erythrocyte Sedimentation Rate.

67.5% of patients show a deterioration, 13.5% an improvement and 18% no change. The relation for those showing deterioration to the previous percentage findings is the same as for the von Bonsdorff count.

C. Delayed Findings. 6. Houghton's Index.

67.5% show a deterioration, 27% an improvement and 4.5% no change. The percentage showing deterioration is 4.5% lower than the antecedent percentage, but 18% lower than the coincident percentage.

Thus, most of the delayed results show that the patients' blood state is now more abnormal than immediately before the onset of the effusion, but less abnormal than indicated by the findings coinciding with the establishment of the effusion. Clinically, this too is usually quite obvious, the patients' condition tending gradually to return to a more satisfactory symptom-free state. That this improvement is in many patients retained, is shown by the average readings noted in the progress counts.

TABLE 32. PROGRESS COUNTS.

	Improvement.	Deterioration.
Total White Cell Count. Number.	15.	7.
Percentage.	67.5.	31.5.
Neutrophils. Number.	13.	9.
Percentage.	58.5.	40.5.
Lymphocyte/Monocyte Ratio. Number.	18.	4.
Percentage.	81.	18.
Von Bonsdorff Count. Number.	10.	12.
Percentage.	45.	54.
Erythrocyte Sedimentation Rate. Number.	16.	6.
Percentage.	72.	27.
Houghton's Index. Number.	11.	11.
Percentage.	49.5.	49.5.

All the factors in the progress haemograms, apart from the von Bonsdorff count and Houghton's Index, show predominantly an improvement in the patients' blood state. It is important to assess precisely the numbers and corresponding/

corresponding percentages in which the progress counts agree with the clinical state.

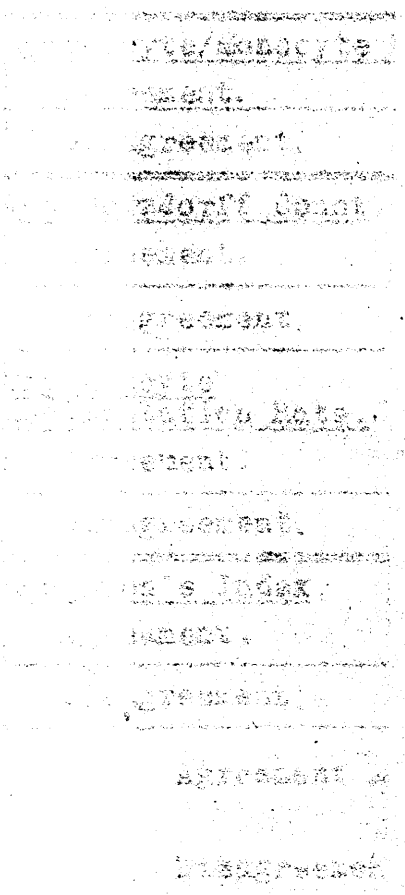


Table 33. Progress Counts compared with Clinical Condition.

	Non-Effusion Group.				Effusion Group.			
	Improvement.		Deterioration.		Improvement.		Deterioration.	
	No.	%	No.	%	No.	%	No.	%
Total White Cell Count.								
Agreement.	22.	100.	2.	67.	14.	93.	9.	90.
Disagreement.	0.	0.	1.	33.	1.	7.	1.	10.
Neutrophils.								
Agreement.	21.	95.	3.	100.	15.	100.	9.	90.
Disagreement.	1.	5.	0.	0.	0.	0.	1.	10.
Lymphocyte/Monocyte Ratio.								
Agreement.	21.	95.	2.	67.	15.	100.	7.	70.
Disagreement.	1.	5.	1.	33.	0.	0.	3.	30.
Von Borsdorff Count.								
Agreement.	22.	100.	2.	67.	15.	100.	9.	90.
Disagreement.	0.	0.	1.	33.	0.	0.	1.	10.
Erythrocyte Sedimentation Rate.								
Agreement.	21.	95.	2.	67.	13.	86.	9.	90.
Disagreement.	1.	5.	1.	33.	2.	14.	1.	10.
Houghton's Index.								
Agreement.	21.	95.	3.	100.	13.	86.	10.	100.
Disagreement.	1.	5.	0.	0.	2.	14.	0.	0.

Agreement = Progress counts in agreement with clinical condition.

Disagreement = Progress counts in disagreement with clinical condition.

The results given in the preceding table show a remarkably close agreement between the haemogram and the patients' clinical state, both for the non-effusion and effusion groups. This agreement is most marked when the patient is improving. The very small number of patients showing deterioration in the non-effusion group makes the percentage values of little importance for that particular section of the group.

Among the twenty-five patients of the non-effusion group, five patients each showed a disagreement of one item of the haemogram with the clinical state. Three of these patients (8, C.McD., 18, R.A., 26, E.W.) were deteriorating and two (12, W.J., 24, M.McA.) were improving. Of the twenty-five patients of the effusion group, eight showed a disagreement of the blood findings with the clinical state. Of these patients, five were deteriorating (6, M.J., 7, A. McI., 33, J.L., 36, D.M., 39, M.F) and three improving (22, A.L., 34, A.McN., 44, M.T.). Of the five showing deterioration, three showed disagreement of one item, one of two items and one of three items. Of the three improving, two showed disagreement of two items and one of one item. Over all these eight patients, the Lymphocyte/Monocyte ratio disagreed with the clinical state in four patients, the erythrocyte sedimentation rate in three patients, the white blood cell count and Houghton's Index in two patients each, and the neutrophil percentage

and/

and von Bonsdorff count in two patients each.

It would appear that the individual findings of the haemogram have a much closer correlation with the clinical condition of the patient over the period when progress counts are being performed, than during the phase when the complication of pleural effusion is occurring. Of the non-effusion group, 20% showed disagreement of the haemogram with the clinical state, the corresponding figure for the effusion group being 32%. Morris and Wilson (145) found disagreement between the haemogram and the clinical state of their patients in 25% of cases. Stobie, England and McMenemy (113) found that during artificial pneumothorax therapy, only the improved patients recorded a definite change in the haemogram, and that this occurred in only one third of these patients. Stationary patients showed a number of definite changes, up to 50% showing improvement. An error of 10% was recorded for patients deteriorating. Behr(146) found the Crawford Index to be fallacious in 50% of patients. Thus it seems that the findings of various writers differ considerably. This applies not only to all the items of the haemogram considered collectively in the form of an index, but also to the individual items. It is therefore not surprising that some workers stress one item of the haemogram, which, in their investigations, has/

has had a close agreement with clinical findings, while others stress a different item. The tendency to do this was noted previously in the section preceding the presentation of the writer's own results.

As was mentioned in the preparation of Table 31, the time factor was one of the difficulties encountered. In order to assess the value of the haemogram findings farther, Table 34 is presented, giving the duration in days of the change in these findings before the onset of an effusion, and also the duration of the preceding symptoms and signs.

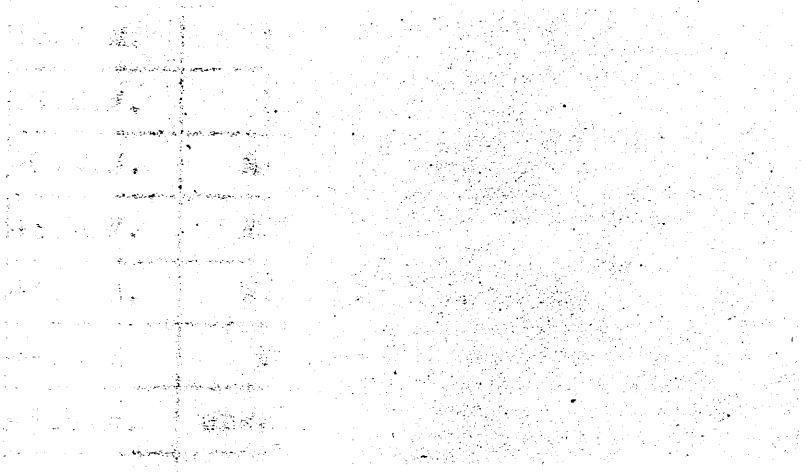


Table 34. Duration in days of change in blood findings and in symptoms and signs before onset of effusion.

No. and Initials.	Total White Cell Count.	Neutrophils.	Lymphocyte/ Monocyte Ratio.	Von Bonsdorff Count.	Erythrocyte Sedimentation Rate.	Houghton's Index.	Symptoms and Signs.
3.M.P.	C.	112.	112.	84.	112.	112.	2.
4.A.McN.	N.S.	N.S.	C.	2.	2.	2.	2.
5.C.H.	N.S.	2.	N.S.	C.	2.	2.	none.
6.M.J.	N.S.	N.S.	N.S.	12.	N.S.	12.	10.
7.A.McI.	5.	N.S.	C.	C.	5.	5.	12.
9.M.B.	N.S.	C.	C.	C.	C.	C.	4.
10.M.McA.	N.S.	C.	N.S.	N.S.	N.S.	C.	22.
13.G.McC.	N.S.	C.	C.	C.	C.	14.	C.
14.E.S.	20.	20.	20.	20.	20.	20.	16.
15.E.W.	8.	26.	8.	N.S.	8.	26.	8.
22.A.L.	C.	C.	C.	C.	C.	C.	none
23.M.B.	C.	C.	C.	6.	6.	6.	17.
29.J.W.	8.	N.S.	N.S.	N.S.	10.	N.S.	10.
31.A.F.	C.	C.	N.S.	11.	C.	11.	7.
32.A.K.	N.S.	N.S.	C.	C.	C.	C.	none
34.A.McN.	7.	C.	C.	C.	C.	9.	7.
35.J.L.	8.	C.	N.S.	8.	8.	8.	none
36.D.M.	14.	28.	14.	28.	28.	28.	34.
39.M.F.	7.	N.S.	N.S.	N.S.	7.	7.	7.
40.M.M.	N.S.	N.S.	N.S.	C.	C.	C.	none
42.M.W.	N.S.	N.S.	N.S.	C.	C.	C.	none
43.J.B.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	6.
44.M.P.	C.	C.	C.	C.	C.	C.	4.
45.M.R.	unknown.	unknown.	unknown.	unknown.	unknown.	unknown.	unknown.
47.J.B.	6.	N.S.	N.S.	6.	N.S.	4.	4.

N.S. = Not Significant.
C. = Coincident.

TABLE 35.

Summary of Table 34, giving number and percentage of patients showing antecedent, coincident, or no significant change in blood findings and symptoms. (24 patients)

	Antecedent.		Coincident.		Not significant.	
	No.	%	No.	%	No.	%
Total White Cell Count.	9.	37.	5.	21.	10.	42.
Neutrophils	5.	21.	9.	37.	10.	42.
Lymphocyte/ Monocyte ratio.	4.	17.	9.	37.	11.	46.
Von Bonsdorff Count.	9.	37.	10.	42.	5.	21.
Erythrocyte Sedimentation Rate.	11.	46.	10.	42.	3.	12.
Houghton's Index.	15.	63.	7.	29.	2.	8.
Symptoms.	17.	71.	1.	4.	6.	25.

It is evident from Table 34, that there is a wide range in the time preceding the onset of an effusion during which symptoms and signs and changes in the haemogram appear. Some patients show no change till the effusion is appearing, whereas, at the opposite extreme, is one patient showing a change in some of the items of the haemogram 112 days prior to the effusion, these changes not being due to any other known cause. However, most

of/

of the alterations in the blood findings appear in the month preceding the effusion. The order in which the changes most often appear is, symptoms and signs (71%), Houghton's Index (63%), erythrocyte sedimentation rate (46%), total white cell count and von Bonsdorff count (each 37%), neutrophil percentage (21%), and Lymphocyte/ Monocyte ratio (17%). These findings are not in agreement with those previously mentioned by Duffy in estimating activity in pulmonary tuberculosis. The order he gives is (1) leucocytic reactions, (2) erythrocyte sedimentation rate, (3) X-ray shadows, (4) signs and symptoms. In the writer's series the patients with unilateral disease who show an antecedent change in some blood factor are six out of a total of nine; for bilaterally diseased patients, the corresponding figure is ten out of a total of fifteen. The percentage figure for each group is therefore 66%.

As noted above, it is the presence of new symptoms and signs, prior to the development of a pleural effusion, which has a higher percentage value than any of the items of the haemogram.

TABLE 36.

(applies to 24 patients).

	Number.	Percentage.
No. of times Total White Cell Count rise preceded symptoms and signs.	4.	16.
No. of times Neutrophil rise preceded symptoms and signs.	4.	16.
No. of times Lymphocyte/Monocyte ratio fall preceded symptoms and signs.	2.	8.
No. of times von Bonsdorff Count fall preceded symptoms and signs.	5.	20.
No. of times Erythrocyte Sedimentation Rate rise preceded symptoms and signs.	4.	16.
No. of times Houghton's Index fall preceded symptoms and signs.	9.	37.

Table 36 shows the number of times that a deterioration in each item of the haemogram preceded these new symptoms and signs. The corresponding percentage figures are also given, and clearly demonstrate that the percentage of patients showing a change in the haemogram before the onset of symptoms and signs, does not justify the time and labour expended on blood examinations.

Conclusions/

Conclusions.

(1) The haemogram is less often of value in the detection of an impending complication than are symptoms and signs.

(2) The order of value of the individual blood findings in the early detection of a complication is:-

(a) Houghton's Index.

(b) Erythrocyte Sedimentation rate.

(c) Total white blood cell count.

(d) Von Bonsdorff count.

(e) Neutrophil count.

(f) Lymphocyte/Monocyte ratio.

Only Houghton's Index indicates deterioration in over 50% of patients.

(3) The highest correlation between the haemogram and the clinical findings is found in the progress counts.

(4) The clinical value of the data obtained by the examination of the blood of patients before, during and after the development of a pleural effusion during artificial pneumothorax therapy, does not justify the time spent in performing this work.

The Haemogram in Patients developing Tuberculous Empyemata.

It will be of interest to compare the blood findings in the eleven of Group Y patients who developed empyemata, with the corresponding results in the patients whose serous effusion did not progress to empyema formation. The numbers involved are small and the accuracy of the findings consequently impaired. Two patients (32, A.K., 42, M.W.), who developed empyemata, are omitted from the table given, for they had small collections of fluid in the pleural space when blood examinations were commenced. One patient (45, M.R.), who developed a serous effusion after dismissal from hospital, is also omitted as no blood findings are available at the onset of her effusion. The number considered is therefore thirteen for the serous effusion group and nine for the empyema group. The figures given in Table 37 are percentages to the nearest whole number.

Table 37.

	Total White Cell Counts.		Neutrophils.		Lymphocyte/ Monocyte Ratio.		Von Bonsdorff Count.		Erythrocyte Sedimentation Rate.		Houghton's Index.	
	S.G.	E.G.	S.G.	E.G.	S.G.	E.G.	S.G.	E.G.	S.G.	E.G.	S.G.	E.G.
Antecedent findings.												
No change.	23.	11.	30.	22.	15.	22.	7.		30.	22.		22.
Deterioration.												
Minimal.	15.	22.	23.	11.	30.	22.	7.	33.	7.	44.	15.	44.
Moderate.		33.	15.		15.	22.	15.		23.	22.	23.	11.
Maximal.		11.	7.		7.		23.		15.		23.	
Improvement.	61.	22.	23.	66.	30.	33.	46.	66.	23.	11.	38.	22.
Coincident findings.												
No change.	15.	11.	38.	55.	23.	22.	7.	11.	7.	33.		
Deterioration.												
Minimal.	23.		7.		7.	22.	30.	11.	23.		23.	
Moderate.	15.	22.			15.	11.	15.	11.	38.	33.	23.	22.
Maximal.		22.	7.		23.		15.	22.	15.	22.	38.	44.
Improvement.	46.	44.	46.	33.	30.	44.	30.	44.	15.	11.	15.	33.
Delayed findings.												
No change.	15.	22.	7.	33.	15.	22.		11.	30.	22.	7.	
Deterioration.												
Minimal.	38.	11.	7.	11.	30.	11.	23.	11.	7.			
Moderate.		11.	30.		7.	11.	7.	11.	23.	22.	23.	33.
Maximal.	7.	22.	23.		30.		23.	11.	30.	33.	61.	11.
Improvement.	38.	33.	30.	55.	15.	55.	46.	55.	7.	22.	7.	55.
Progress counts.												
Improvement.	38.	44.	53.	55.	77.	77.	53.	33.	46.	22.	46.	33.
Deterioration.	61.	55.	46.	44.	23.	23.	46.	66.	53.	77.	53.	66.

S.G. = Serous Group.

E.G. = Empyema Group.

Comment.

1. Total white blood cell count.

At the onset of a pleural effusion, it is obvious from Table 37 that there is more often a deterioration in the total leucocyte count in the group of empyemata, and this deterioration is more severe also in the empyema group. Only 38% of the serous effusion group show improvement in the progress counts, whereas 44% of the empyema group show a similar change. This can be accounted for by the fact that, clinically, more patients having serous effusions deteriorated than did those having empyemata. 38% of the first group deteriorated, whereas only 33% of the empyema group deteriorated.

2. Neutrophils.

The serous group shows more often than the empyema group a deterioration in the neutrophil count at the onset of an effusion, and this deterioration is more severe in the first group. The progress counts are very similar in the percentages recording improvement and deterioration for the two groups. This count therefore cannot be taken to have much value in assessing the future trend of the effusion.

3. The Lymphocyte/Monocyte ratio.

The findings also show a preponderance in values indicating a deterioration in the blood findings in the serous/

serous effusion group at the onset of an effusion, and the progress counts show exactly similar percentages. These results are again not of any value in indicating which patients will develop the more serious complication of empyema formation.

4. Von Bonsdorff count.

This count shows more constant and more severe deterioration in the serous effusion group at the onset of an effusion, and the progress counts show more often a deterioration in the empyema group. These findings are difficult to evaluate.

5. Erythrocyte sedimentation rate.

Immediately before the onset of an effusion, the serous effusion group shows a higher percentage of patients showing a severe deterioration in the erythrocyte sedimentation rate, but the empyema group shows a higher percentage showing deterioration altogether. As the effusion becomes established, a higher percentage of the first group shows deterioration, and severe deterioration occurs in approximately equal percentages in both groups. The progress counts indicate that the erythrocyte sedimentation rate remains unsatisfactory in a higher percentage in the empyema groups.

6. Houghton's Index.

The findings for this index closely parallel those of the erythrocyte sedimentation rate.

The results are conflicting and contrary to expectations. The frequency and severity of deterioration in the blood findings at the onset of an effusion which, as it transpired, remains serous, are more marked than at the onset of an effusion which later becomes purulent. The white blood cell count alone is an exception to this. The progress counts usually indicate improvement more often in the serous effusion group than in the empyema group. This finding might be thought to be of considerable value in following the change of character in the effusion, till one considers that clinically the serous group more often showed deterioration than the empyema group.

It may be objected that in the preceding considerations the writer has stated only relative findings. This is fully recognised, but the writer feels that in assessing whether or not a complication is developing, can best be discovered by this method. However, to amplify the subject farther, a record of the absolute blood findings in patients developing empyemata and those not doing so, will be given. The readings chosen for comparison are those observed during the development of the effusion and those recorded four months later. This latter time was fixed at four months, since it was found that, on the average, those patients who developed an empyema did so three to five months after the onset of

a/

a serous effusion. One patient (13, G.McC.) had the second reading taken at one month, since her artificial pneumothorax was abandoned and she was discharged. Two patients (6, M.J., 39, M.F.) had readings taken at three months, and another two (35, J.L., 36, D.M.) at three and a half months (one died, one was discharged irregularly, and the artificial pneumothorax was abandoned in two).

Table 38a. Findings at onset of an effusion.

(1) Serous effusion Group.

No. and initials.	Total White Cell Count.	Neutrophils.	Lymphocyte/ Monocyte Ratio.	Von Bonsdorff Count.	Erythrocyte Sedimentation Rate.	Houghton's Index.
3.M.P.	8,400.	66.	$\frac{1.8}{1.}$	215.	41.	140.
4.A.McN.	9,800.	65.5.	$\frac{2}{1.}$	230.	60.	140.
5. C.H.	8,600.	68.	$\frac{4}{1.}$	252.	13.	216.
6. M.J.	8,400.	62.	$\frac{3}{1.}$	174.	27.	124.
7. A.McI.	10,400.	65.	$\frac{1.6}{1.}$	176.	85.	58.
9. M.B.	12,700.	65.	$\frac{3}{1.}$	150.	41.	198.
10.M.McA.	6,600.	51.	$\frac{5}{1.}$	165.	49.	136.
13.G.McC.	8,800.	54.5.	$\frac{5.3}{1.}$	186.	16.	185.
14.E.S.	11,800.	60.	$\frac{3.5}{1.}$	228.	28.	205.
31.A.F.	12,400.	71.5.	$\frac{2.5}{1.}$	182.	69.	73.
35.J.L.	6,000.	75.	$\frac{1.1}{1.}$	200.	59.	77.
40.M.M.	9,900.	71.	$\frac{1.8}{1.}$	200.	32.	116.
44.M.T.	16,000.	73.	$\frac{1.5}{1.}$	204.	51.	105.
45.M.R.	unknown.	unknown.	unknown.	unknown.	unknown.	unknown.
Range.	6,000 to 16,000.	51 to 75.	$\frac{1.1}{1.}$ to $\frac{5.3}{1.}$	150 to 252.	13 to 85.	58 to 216.
Average.	9,984.	65.2.	$\frac{2.8}{1.}$	197.	44.	136.

Table 38a. Findings at onset of effusion.

(2). Empyema Group.

No. and Initials.	Total White Cell Count.	Neutrophils.	Lymphocyte/ Monocyte Ratio.	Von Bonsdorff Count.	Erythrocyte Sedimentation Rate.	Houghton's Index.
15.E.W.	7,200.	73.	$\frac{4}{1.}$	178.	73.	69.
22.A.L.	13,000.	59.5.	$\frac{3}{1.}$	201.	115.	78.
23.M.B.	20,400.	69.5.	$\frac{1.5}{1.}$	194.	77.	69.
29.J.W.	10,400.	62.5.	$\frac{3}{1.}$	198.	62.	122.
32.A.K.	10,400.	50.5.	$\frac{1.2}{1.}$	172.	80.	78.
34.A.McN.	12,200.	76.5.	$\frac{1.3}{1.}$	226.	62.	105.
36.D.M.	10,200.	84.5.	$\frac{2}{1.}$	214.	41.	103.
39.M.F.	15.400.	73.5.	$\frac{3}{1.}$	162.	31.	91.
42.M.W.	9,400.	60.	$\frac{2.6}{1.}$	178.	83.	132.
43.J.B.	9,000.	78.	$\frac{1.5}{1.}$	236.	50.	172.
47.J.B.	5,400.	59.5.	$\frac{4.1}{1.}$	204.	30.	167.
Range.	5,400 to 20,400.	50.5 to 84.5.	$\frac{1.3}{1.}$ to $\frac{41.}{1.}$	162 to 236.	30 to 115.	69 to 167.
Average.	11,182.	67.9.	$\frac{2.5}{1.}$	196.	55.	104.

Table 38b. Readings four months later.

(1). Serous effusion group.

No. and initials.	Total White Cell Count.	Neutrophils.	Lymphocyte/ Monocyte Ratio.	Von Bonsdorff Count.	Erythrocyte Sedimentation Rate.	Houghton's Index.
3. M.P.	8,800.	76.5.	$\frac{7}{1}$.	201.	57.	105.
4.A.McN.	6,800.	61.5.	$\frac{5}{1}$.	221.	9.	208.
5.C.H.	8,000.	61.5.	$\frac{2.5}{1}$.	259.	5.	227.
6.M.J.	10,200.	88.	$\frac{4.75}{1}$.	184.	31.	81.
7.A.McI.	12,000.	71.5.	$\frac{1}{1}$.	207.	63.	91.
9.M.B.	12,400.	61.5.	$\frac{6.5}{1}$.	255.	3.	254.
10.M.McA.	12,800.	54.	$\frac{3}{1}$.	214.	8.	208.
13.G.McC.	10,200.	56.	$\frac{4}{1}$.	213.	9.	212.
14.E.S.	11,700.	52.5.	$\frac{6.5}{1}$.	234.	21.	236.
31.A.F.	13,900.	59.5.	$\frac{1.75}{1}$.	130.	57.	47.
35.J.L.	12.400.	75.	$\frac{1.5}{1}$.	184.	84.	45.
40.M.M.	12,400.	73.5.	$\frac{5}{1}$.	184.	25.	126.
44.M.T.	15,600.	64.5.	$\frac{2.8}{1}$.	183.	18.	143.
45.M.R.	unknown.	unknown.	unknown.	unknown.	unknown.	unknown.
Range.	6,800 to 13,900.	52.5 to 76.5.	$\frac{1}{1}$ to $\frac{7}{1}$.	130 to 259.	3 to 84.	45 to 254.
Average.	11,324.	65.8.	$\frac{3.9}{1}$.	205.	30.	152.5.

Table 38b. Readings four months later.

(2) Empyema Group.

No. and initials.	Total White Cell Count.	Neutrophils.	Lymphocyte/ Monocyte Ratio.	Von Bonsdorff Count.	Erythrocyte Sedimentation Rate.	Houghton's Index.
15.E.W.	8,800.	67.	$\frac{4}{1}$.	218.	25.	172.
22.A.L.	9,800.	72.5.	$\frac{4}{1}$.	191.	79.	78.
23.M.B.	8,200.	68.	$\frac{2.2}{1}$.	211.	23.	154.
29.J.W.	14,000.	66.	$\frac{3}{1}$.	229.	30.	173.
32.A.K.	11,800.	63.5.	$\frac{4.5}{1}$.	203.	18.	177.
34.A.McN.	11,400.	71.	$\frac{1.9}{1}$.	224.	72.	112.
36.D.M.	10,000.	69.5.	$\frac{2.5}{1}$.	160.	42.	91.
39.M.F.	11,400.	69.5.	$\frac{3}{1}$.	165.	31.	101.
42.M.W.	8,000.	62.	$\frac{2.5}{1}$.	205.	26.	164.
43.J.B.	17,000.	78.	$\frac{1.1}{1}$.	143.	72.	7.
47.J.B.	7,200.	56.5.	$\frac{3.25}{1}$.	188.	24.	165.
Range.	7,200 to 17,000.	56.5 to 78.	$\frac{1.1}{1}$. to $\frac{4}{1}$.	143 to 229.	18 to 79.	7 to 177.
Average.	10,690.	67.6.	$\frac{2.9}{1}$.	194.	40.	126.7

Comment on Findings.

1. Total White Cell Count.

In the serous effusion group, the range of this count is less than that of the empyema group for both readings. In addition, the average reading is higher in the empyema group at the first reading but not at the second. The difference is 1,198 and 634 cells per cubic millimetre respectively. A difference so small as this is hardly significant. It is interesting that the average reading in the serous effusion group rose by 1,340 cells per cmm., while in the empyema group it fell by 492 cells per cmm., at the second reading. This is contrary to what one might expect and cannot be explained by the incidence of bilateral pulmonary tuberculosis in those two groups, for more bilateral cases occurred in the empyema group.

Thus, generally, the total white cell count gives no clear indication whether a patient will later develop an empyema, and it does not reflect this change in the character of the effusion when empyema formation occurs.

2. Neutrophil Count.

The range of the neutrophil count is greater at the first reading in the empyema group, but at the second reading, the range is smaller and not significantly different/

different between the two groups. The average count is only slightly higher in the empyema group both at the first and second readings, and shows a change of less than one per cent. between the first and second readings in each group.

The neutrophil count is thus of no help in assessing whether an empyema will occur as judged by the neutrophil percentage at the onset of the effusion. Also, it gives no indication of the change in the character of the fluid later.

3. Lymphocyte/Monocyte ratio.

The range is lower in the empyema group at both readings and the average reading is also lower in the empyema group. There is a significant improvement in the average Lymphocyte/Monocyte ratio in the serous effusion group at the second reading, and the empyema group shows a slight improvement too.

It would seem that the Lymphocyte/Monocyte ratio is more sensitive as an indicator of empyema formation from a consideration of both the initial and progress readings.

4. Von Bonsdorff count.

The range of the von Bonsdorff count is less in the empyema group for both readings. There is no significant difference in the first readings in the two groups, but the second reading shows a slight improvement in the serous effusion/

effusion group and a very slight deterioration in the empyema group. The average reading for the empyema group is lower.

The first reading is of little value in predicting if an empyema will occur, and the progress reading is not of significant value, although the serous effusion group shows some improvement.

5. Erythrocyte Sedimentation Rate.

The range of the one hour erythrocyte sedimentation rate value is greater in the empyema group at the first reading, but not at the second reading, compared with that of the serous effusion group. The average reading is higher in the empyema group on both occasions. Both groups show improvement in the average value of the second reading.

It would appear that the erthrocyte sedimentation rate might be of some value in assessing the severity of the pathological process in these two groups.

6. Houghton's Index.

The range of Houghton's Index is greater in the serous effusion group at both first and second readings. The average value is significantly lower in the empyema group at both readings, but shows improvement in both groups/

groups at the second reading. Houghton's Index would seem to have a similar value to the erthrocyte sedimentation rate.

The Lymphocyte/Monocyte ratio, the erythrocyte sedimentation rate and Houghton's Index are of most value in assessing whether an empyema will occur as a sequel to a serous effusion, as judged by the average values found during the development of the effusion. Although the average values in the empyema group are less favourable than in the serous effusion group four months after the development of the effusion, there is an improvement in both groups compared with the first reading. Thus, although the change in the blood picture as worked out in Table 37 is of little or no value in forecasting the course of an effusion and in following the course of it, nevertheless, the absolute values of the Lymphocyte/Monocyte ratio, erthrocyte sedimentation rate and Houghton's Index, as noted above, are of some value. It should be noted however, that in six patients of the serous effusion group and in six patients of the empyema group, contralateral disease of sufficient extent to exert an unfavourable influence on the blood picture was present. This impairs the value of the progress counts considerably.

It was previously mentioned that 33% of the empyema group showed clinical evidence of deterioration during the period when their serous effusion was changing

in/

in character. These patients all suffered from bilateral pulmonary tuberculosis and so their blood findings were unfavourably influenced by the contralateral disease. To assess whether the change in character of the fluid per se can produce unfavourable blood findings, it is reasonable to consider progress counts in patients having unilateral pulmonary tuberculosis which, ideally, should be under control. Three patients who developed empyemata in this series had unilateral pulmonary tuberculosis (Group Y, 15, E.W., 23, M.B., 34, A. McN.) and none showed symptoms or signs which might have led one to believe that an empyema was in process of formation. Scrutiny of the serial counts of these three patients reveals that only one (34, A.McN.) showed serial counts which indicated an unsatisfactory condition. His Lymphocyte/Monocyte ratio was persistently low, his erythrocyte sedimentation rate persistently elevated, and his Houghton's index figures were low. This patient's pulmonary tuberculosis was not altogether controlled by his artificial pneumothorax in spite of a ninety per cent. collapse of the lung. On account of copious sputum and a very persistent cough with recurrent clinical bronchitis, it was thought that he had tracheo-bronchial tuberculosis. Thus, the pathological changes in the respiratory tract could have produced the unfavourable blood findings. The previous finding of the/

the very doubtful value of serial haemograms as a guide to the clinician in the conduct of patients having hydro-pneumothorax is therefore still maintained, for neither of the two patients (15, E.W., 23, M.B) whose pulmonary disease was controlled by their pneumothorax, showed evidence in the blood findings which might have led one to suspect empyema formation.

Conclusions.

1. Consideration of the change in the blood findings at the onset of pleurisy with effusion in patients treated by artificial pneumothorax, is of little value in prognosticating the type of effusion which will appear.

2. Serial haemograms are of little value in following the changes which may take place in a serous effusion complicating an artificial pneumothorax.

3. The change in the blood findings at the onset of a pleural effusion, confirms the impression gained in a previous section that there is an exacerbation of tuberculous disease at this time in a majority of patients.

To/

To illustrate the conclusions arrived at on the blood findings in the serous effusion group and in the empyema group, graphs are appended. One patient suffering from unilateral pulmonary tuberculosis, and one suffering from bilateral pulmonary tuberculosis was selected for each group.

Patients having Unilateral Disease.

Patient 10, M.McA.

This patient developed an effusion on 25.10.42. Symptoms and signs indicating that an effusion was about to develop, appeared on 17.10.42. From the graphs, it is seen that at this time no indication of the impending effusion was evident. Certainly the total white blood cell count was markedly abnormal, but it had been so previously. The other findings were showing a tendency to improve apart from the Lymphocyte/Monocyte Ratio which fell from $\frac{4}{1}$ to $\frac{3.5}{1}$
These values for the ratio are not abnormal. The graphs illustrate well the fall in the total white blood cell count with the onset of the effusion, accompanied by a relative increase in the lymphocytes. It is striking that the maximum fall in the Lymphocyte/Monocyte Ratio and in Houghton's Index, and the maximum rise in the erythrocyte sedimentation rate were delayed two to three weeks from the onset of the effusion.

The progress counts up to the point at which pleural obliteration was complete, were, on the whole, not unsatisfactory, considering that the disease had not been controlled by the pneumothorax.
The rise in the total white blood cell count in February, 1943, occurred soon after the patient was allowed up. Medlar (56) found that exercise lowered the total white blood/

blood cell count in five tuberculous patients. The rise in the erythrocyte sedimentation rate and the fall in Houghton's Index which occurred in May, 1943, could not be accounted for clinically.

The sharp rise in the erythrocyte sedimentation rate with a coincident fall in Houghton's Index and the von Bonsdorff count, together with an increased neutrophil percentage and diminished Lymphocyte/Monocyte Ratio which occurred in August and September, 1943, was due to wound sepsis following a first stage thoracoplasty.

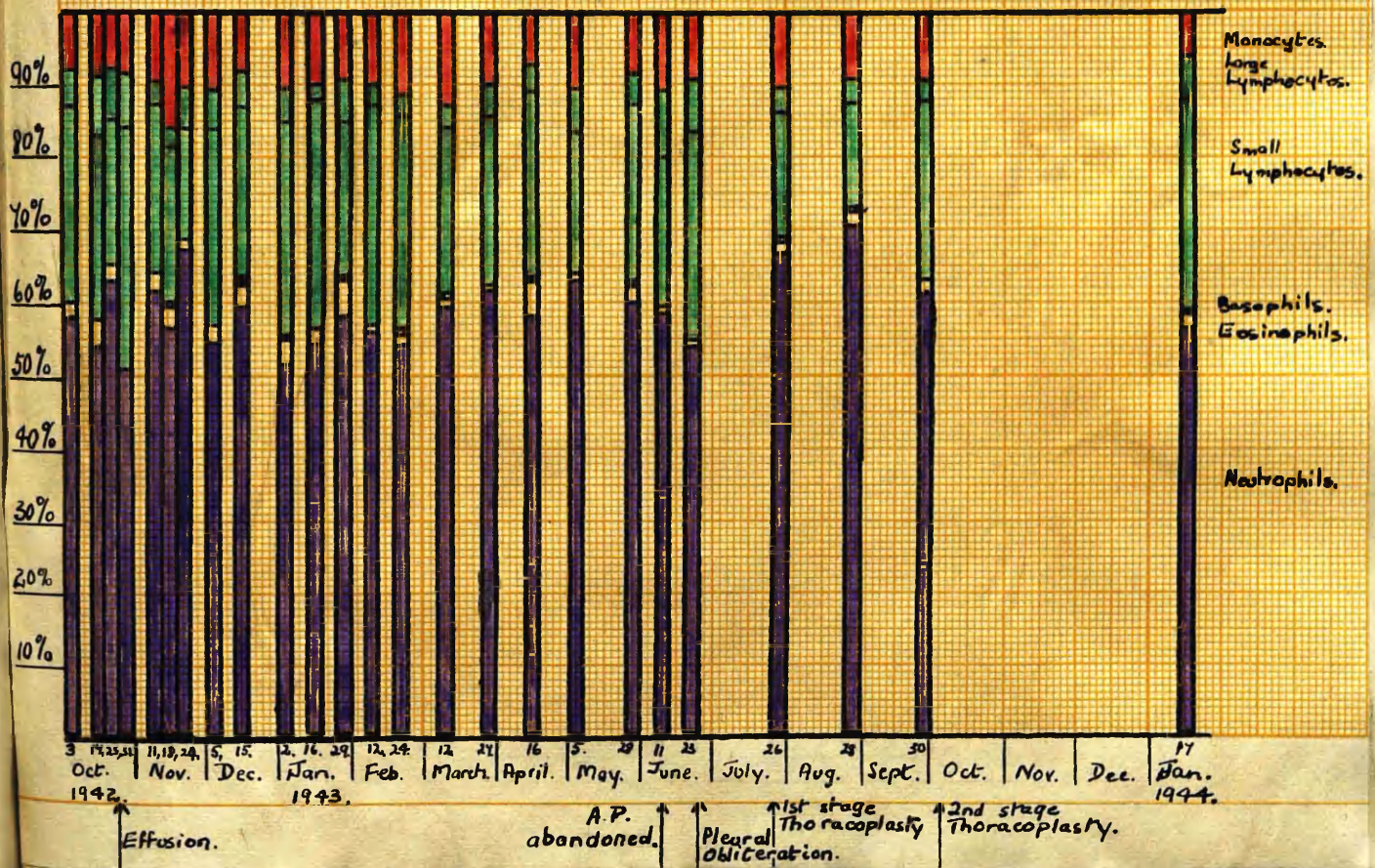
The final readings indicated satisfactory control of the disease following completion of the thoracoplasty. This patient was discharged on 22.1.44.

Comment.

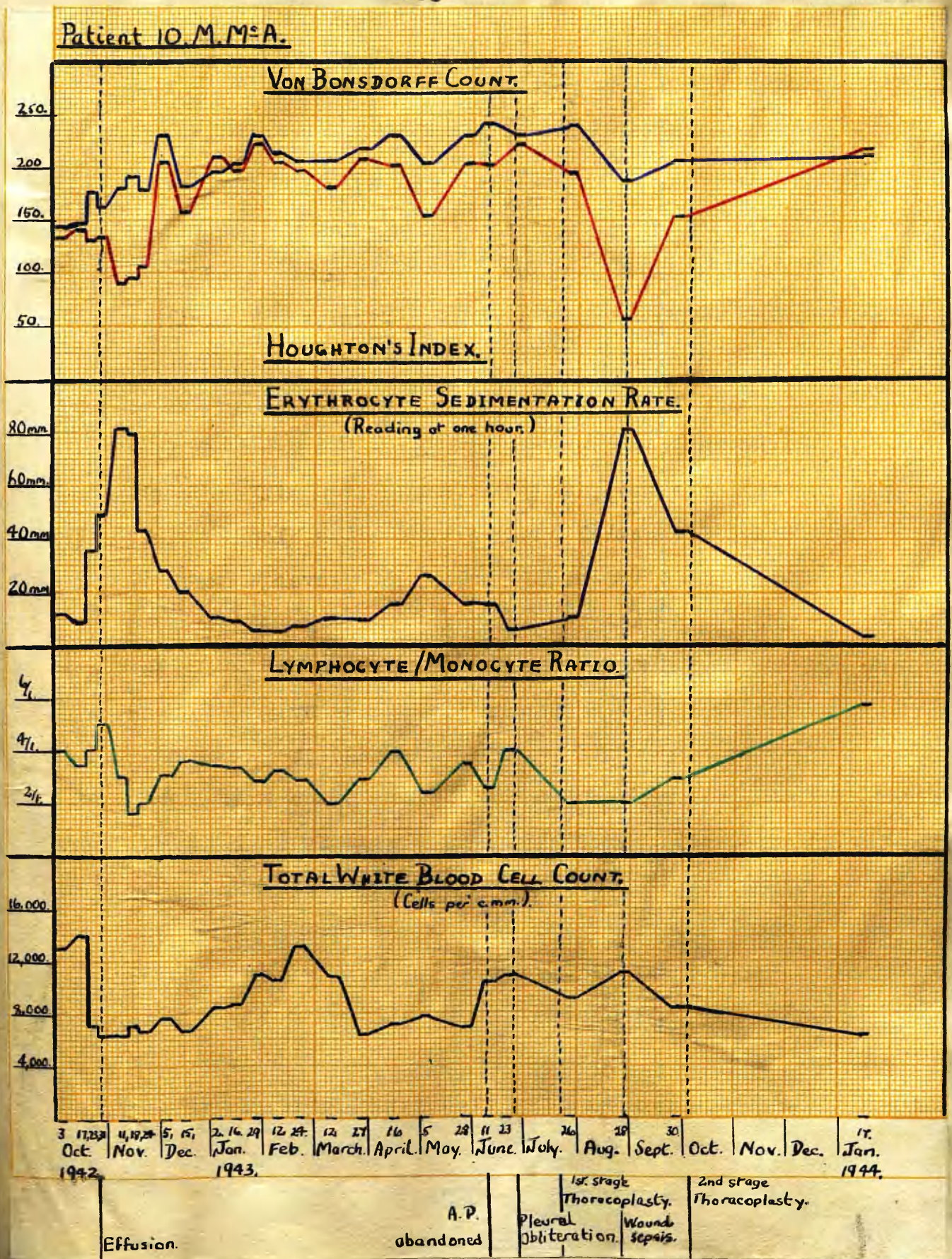
In this patient the blood findings were of no great value at the onset of the effusion. The progress counts only confirmed the clinical findings. The graphs illustrate well the effect of wound sepsis and the satisfactory result of effective collapse therapy.

Patient 10. M. McA.

Differential Leucocyte Count.



Patient 10. M. McA.



Patient 23,M.B.

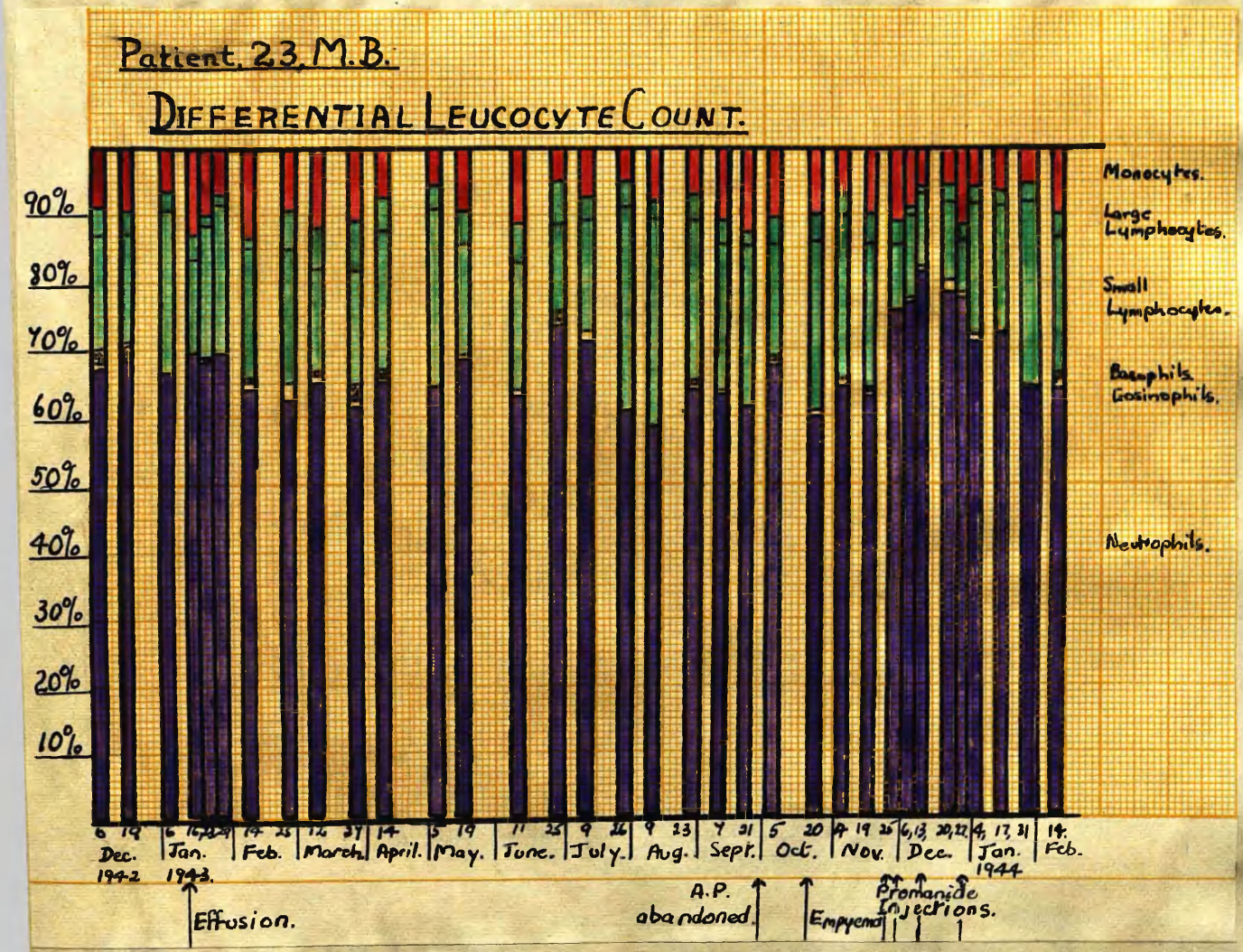
Symptoms and signs suggestive of an impending complication within the pneumothorax, occurred twenty days before the onset of fluid formation. The haemogram values noted, showed in this patient a fall in the total white blood cell count, together with a fall in the Lymphocyte/Monocyte Ratio coincident with the effusion. In this patient the maximum rise in the erythrocyte sedimentation rate, and the maximum fall in Houghton's Index and in the von Bonsdorff Count, occurred more rapidly than in patient 10,M.McA.

The progress counts showed a considerable improvement on the findings at the onset of the effusion, but they indicated that some activity was proceeding. The sharp rise in the neutrophil percentage in June, 1943, could not be accounted for clinically. The rise in the total white blood cell count and in the erythrocyte sedimentation rate, together with a fall in the Lymphocyte/Monocyte Ratio, in the von Bonsdorff Count and in Houghton's Index, which occurred on 21.9.43, could have been caused by an attack of coryza. It is interesting to note that the previous readings on 7.9.43, apart from the Lymphocyte/Monocyte Ratio, were showing evidence of deterioration, for at this time a specimen of fluid aspirated, showed that/

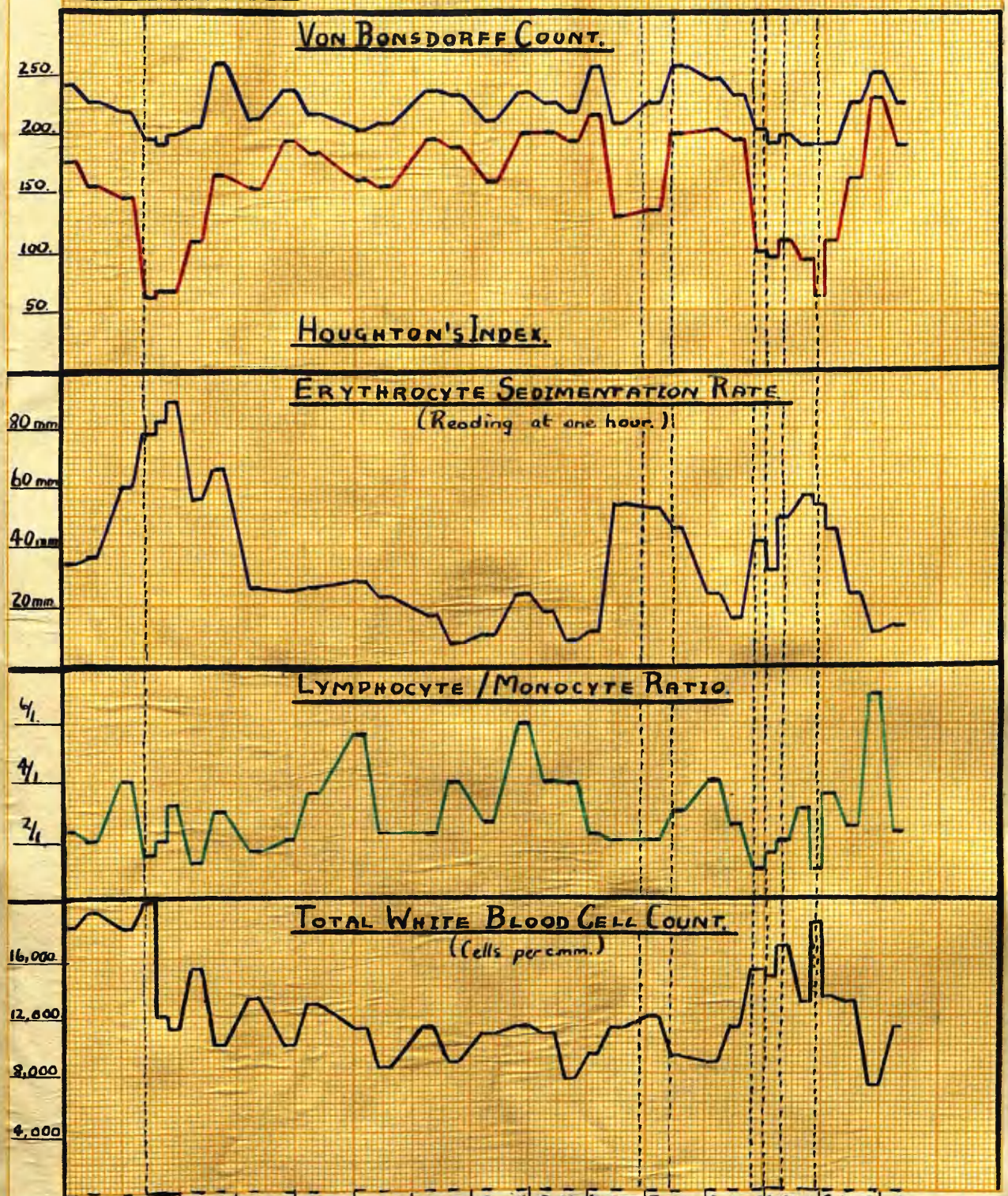
that it was becoming turbid. In addition, the patient was now feeling as well as she previously had been. When frank pus was aspirated on 18.10.43, the haemogram values were again tending to improve. The sharp rise in the total white blood coll count, in the neutrophil percentage and in the erythrocyte sedimentation rate, together with a fall in the Lymphocyte/Monocyte Ratio,in the von Bonsdorff Count and in Houghton's Index, which occurred in November and December, 1943, was due to the introduction of a solution of Promanide into the pleural cavity. This substance which kills tubercle bacilli in guinea-pigs (147), was found to be very toxic when introduced intrapleurally in four of the writer's patients (148). It produced marked general and local reactions, The last injection was given on 20.12.43 to this patient, but it took another month for satisfactory haemogram values to be reached. This patient's pleural cavity finally became obliterated and she went home in good condition on 23.6.44.

Comment.

Again, clinical signs and symptoms are seen to be an earlier indication of impending complications than changes in the haemogram. The graphs illustrate the effect of intercurrent infection and the effect of the introduction of a toxic substance which sets up a chemical pleuritis.


Patient. 23. M.B.
DIFFERENTIAL LEUCOCYTE COUNT.
90%
80%
70%
60%
50%
40%
30%
20%
10%
Monocytes.
Large Lymphocytes.
Small Lymphocytes.
Basophils.
Eosinophils.
Neutrophils.
6 19 Dec. 1942
6 16,23,29 Jan. 1943.
14 25 Feb.
14 March.
14 April.
5 19 May.
11 25 June.
9 16 July.
9 23 Aug.
7 21 Sept.
5 20 Oct.
4 19 26 Nov.
6,13 Dec.
20,27 Jan. 1944
4, 17, 31 Feb.
14.
Effusion.
A.P. abandoned.
Empyema
Promanide Injections.

Patient, 23. M B.



Patients having Bilateral Disease.

Patient 29, J.W.

On 28.10.43, the first clinical indication appeared that all was not well with this patient's pneumothorax. It was not till 8.5.43 that an effusion was noted. A slight increase in the total white blood cell count, with also a slight increase in the neutrophil percentage and in the Lymphocyte/Monocyte Ratio, and a rise of 8mm. in the erythrocyte sedimentation rate, preceded the effusion. Coincident with the effusion, the total white blood cell count fell, the neutrophil percentage fell slightly and so also did the Lymphocyte/Monocyte Ratio; in addition, the erythrocyte sedimentation rate rose sharply, and the von Bonsdorff Count and Houghton's Index showed a sharp fall.

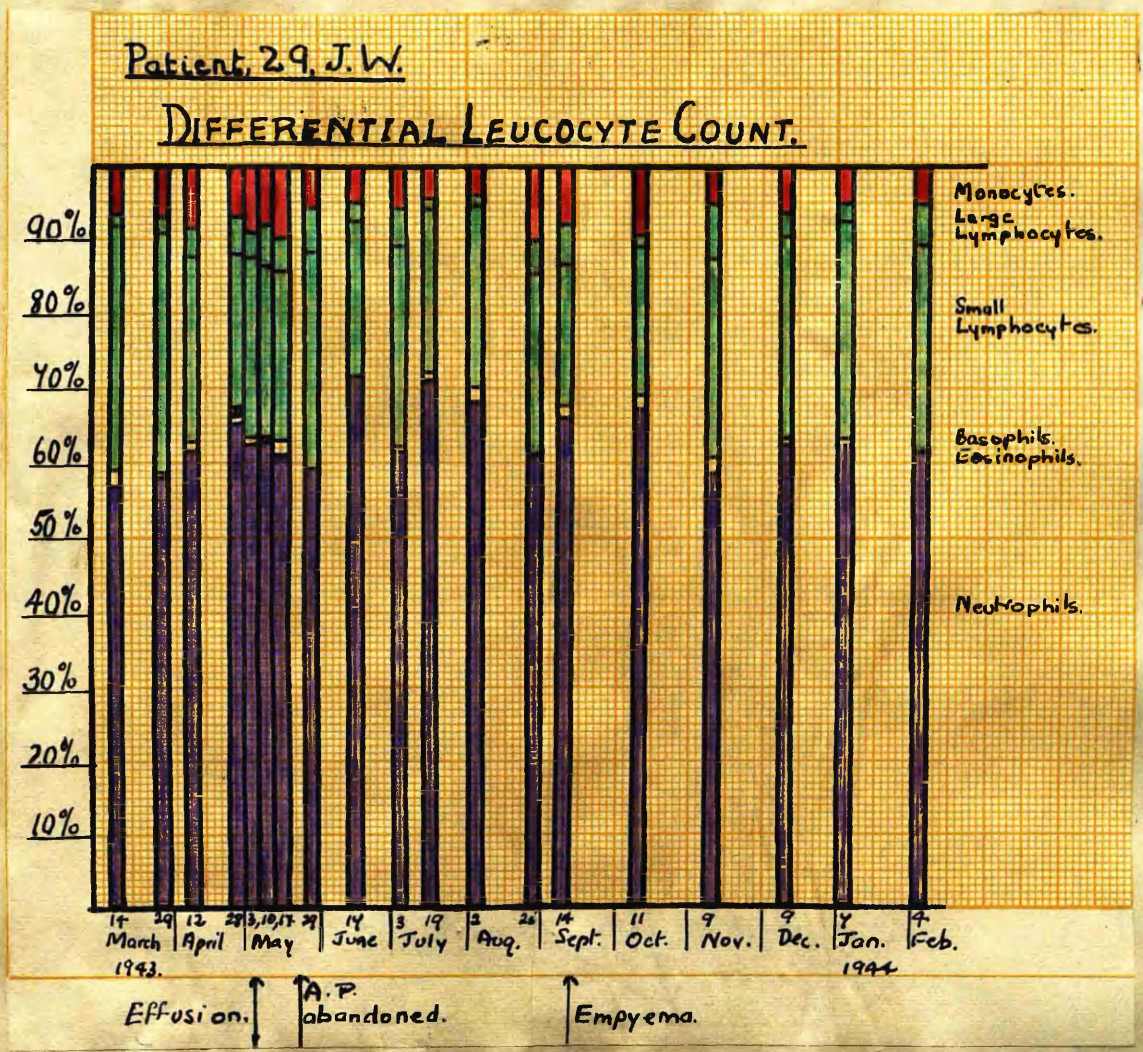
The progress counts, apart from the Lymphocyte/Monocyte Ratio, were slow in returning to satisfactory levels. This was associated with clinical symptoms of a persistent pleurisy. On 5.9.43 purulent fluid was aspirated, and it is rather surprising to find thereafter, comparatively satisfactory readings for the total white blood cell count, the neutrophil percentage and the Lymphocyte/Monocyte Ratio. The erythrocyte sedimentation rate having fallen progressively till pus appeared, promptly began/

began to rise again. The von Bonsdorff Count and Houghton's Index showed little change after the development of pus.

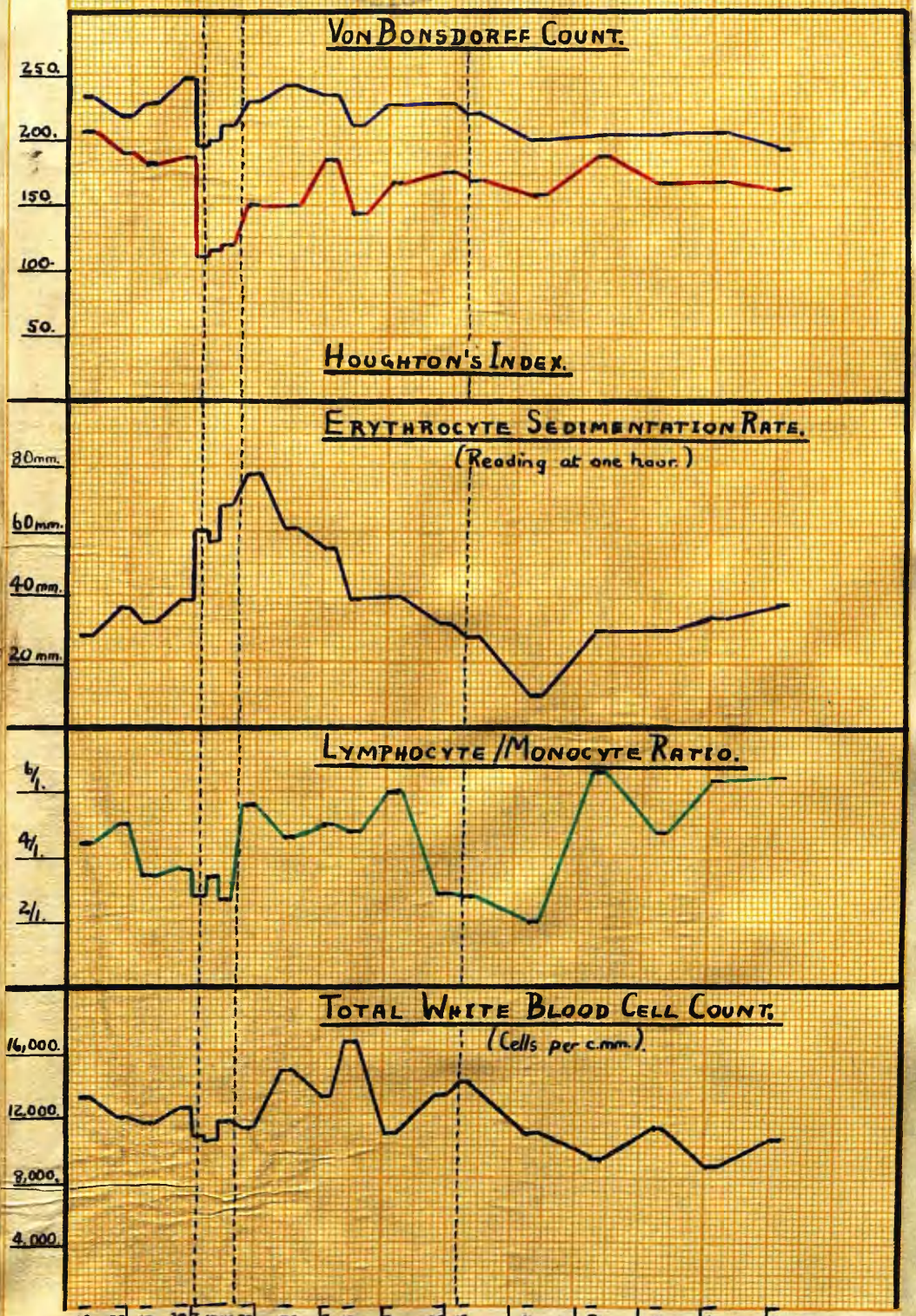
By 20-6-44 pleural obliteration was complete. A two-stage thoracoplasty was later performed with a satisfactory result and the patient was discharged well on 27.9.45.

Comment.

The clinical findings were again of superior value to the haemogram findings. The unsatisfactory progress counts could not be attributed wholly to the change in the character of the effusion, for there was present contralateral disease which was active at this time.


Patient, 29, J.W.
DIFFERENTIAL LEUCOCYTE COUNT.
90%
80%
70%
60%
50%
40%
30%
20%
10%
Monocytes.
Large Lymphocytes.
Small Lymphocytes.
Basophils.
Eosinophils.
Neutrophils.
14 March 1943.
29
12 April
28
3, 10, 17 May
29
14 June
3
19 July
3
26 Aug.
14 Sept.
11 Oct.
9 Nov.
9 Dec.
7 Jan. 1944
4 Feb.
Effusion.
A.P. abandoned.
Empyema.

Patient, 29. J.W.



Patient 31, A.F.

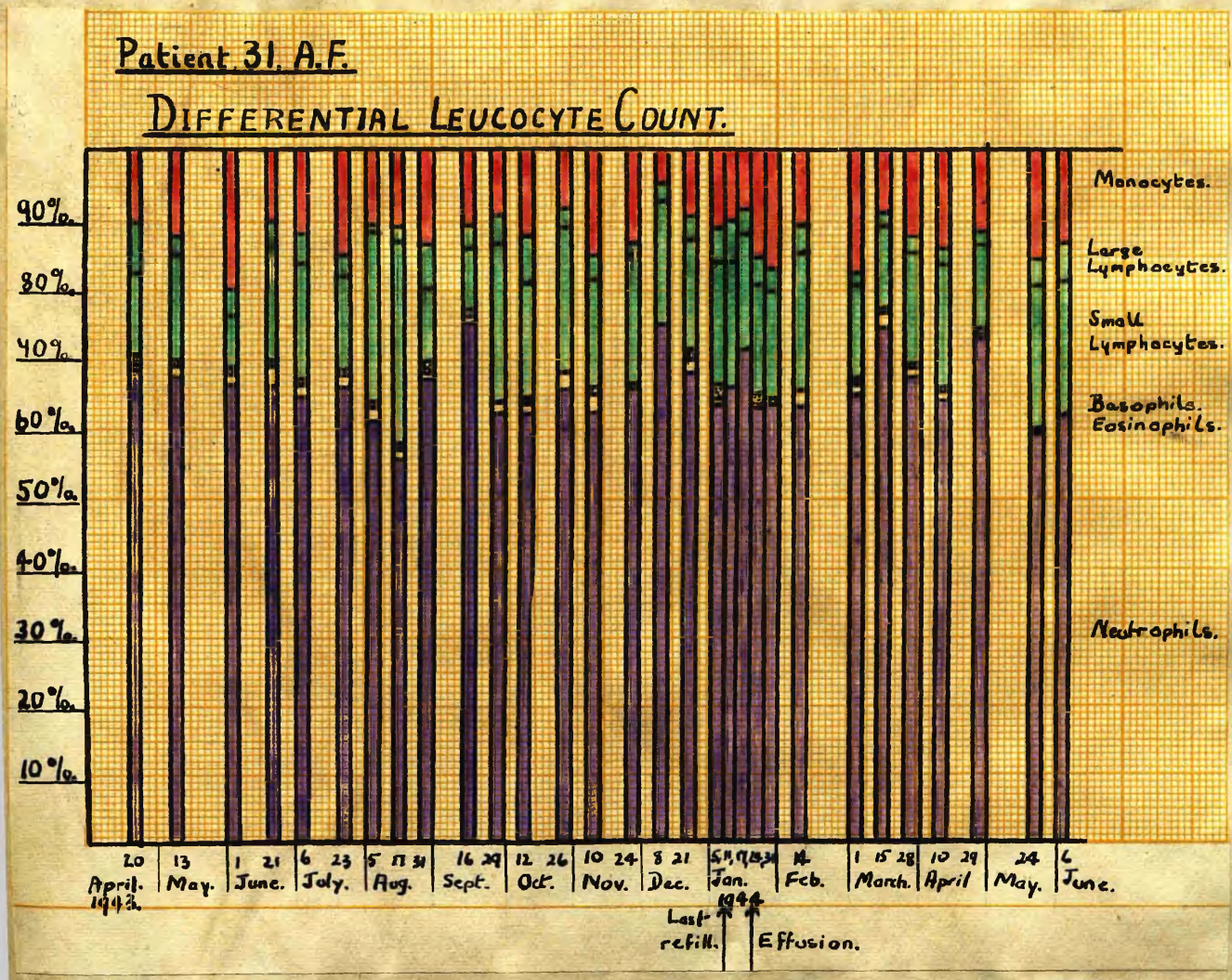
This patient did not develop an effusion till nine and a half months after the induction of her pneumothorax. The disease in the collapsed lung was only partially controlled, and contralateral disease was present and showed no great tendency to improve. The trend of the haemogram findings was obviously unsatisfactory. The marked peaks in the neutrophil percentage which occurred in September and December, 1943, coincided with attacks of coryza.

On 9.1.44 signs and symptoms appeared which suggested that an effusion might occur, and on 16.1.44 an effusion was seen on taking a skiagram with the portable X-ray unit. It is again evident that the deterioration which occurred in all the haemogram findings coincided with, rather than preceded, the onset of fluid formation. The subsequent readings, apart from some of the neutrophil percentage values, were wholly in keeping with the clinical condition of rapid deterioration which ensued following the effusion. It is interesting, however, to note that this patient's effusion ultimately dried up. Pleural obliteration was complete by October 1944. She died on 30.5.45.

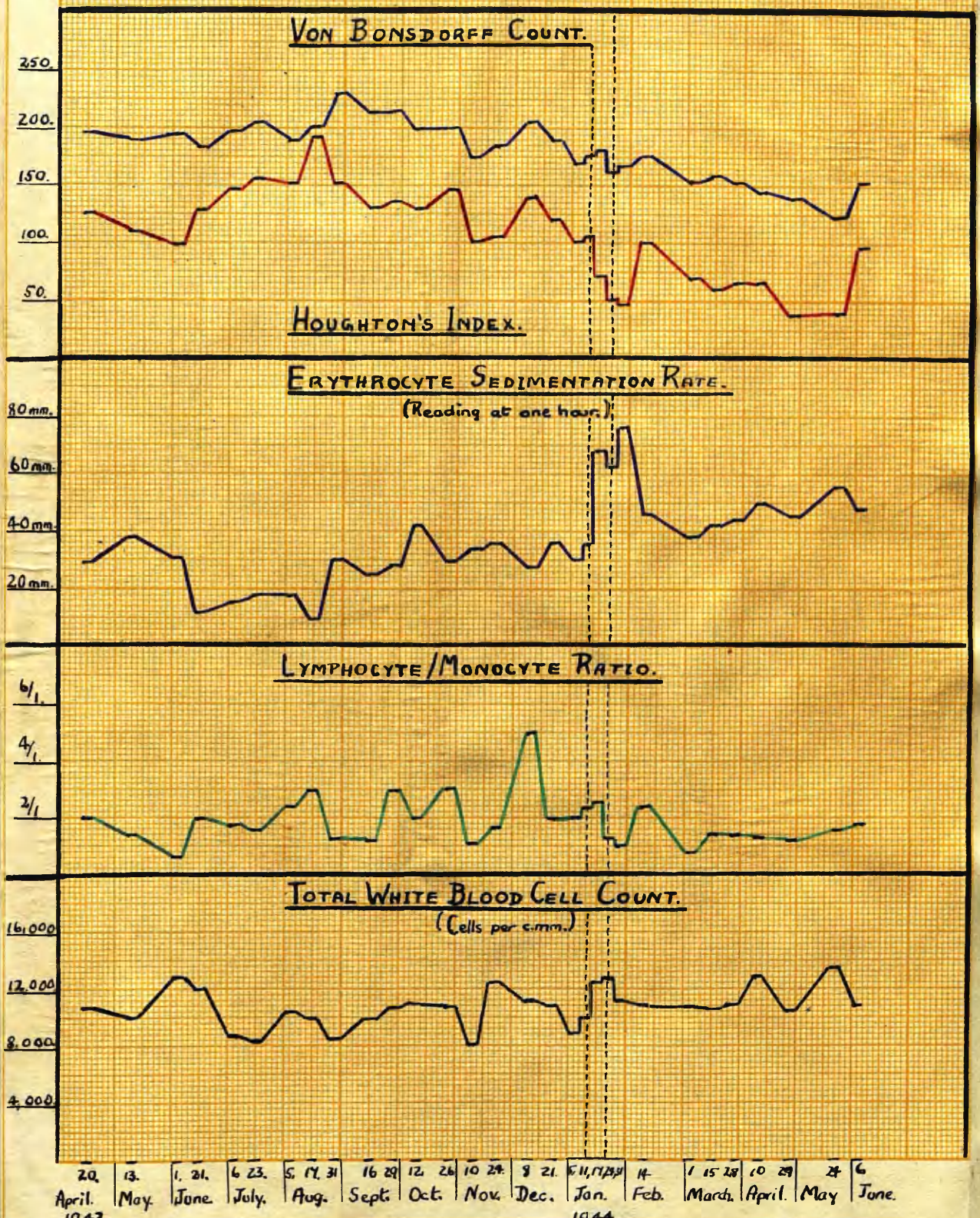
Comment.

In this patient, suffering from bilateral pulmonary/

pulmonary tuberculosis, the blood findings proved of little assistance, confirming only the clinical findings. Should empyema formation have occurred, it would probably not have been detected from the haemogram findings which were already indicative of a deterioration in the patient's condition.


Patient 31. A.F.
DIFFERENTIAL LEUCOCYTE COUNT.
90%.
80%.
40%.
60%.
50%.
40%.
30%.
20%.
10%.
Monocytes.
Large Lymphocytes.
Small Lymphocytes.
Basophils. Eosinophils.
Neutrophils.
20 April. 1943.
13 May.
1 21 June.
6 23 July.
5 17 31 Aug.
16 29 Sept.
12 26 Oct.
10 24 Nov.
8 21 Dec.
5 11 19 26 31 Jan. 1944
14 Feb.
1 15 28 March.
10 29 April
24 May.
6 June.
Last refill.
Effusion.

Patient. 31. A.F.



The End Results of Artificial Pneumothorax Treatment.

Although the main purpose of this investigation has been to elucidate the aetiology of pleural effusions which occur during artificial pneumothorax therapy, and to assess the value of serial blood examinations in relation to such effusions, it would not be satisfactorily completed were the end results of treatment not recorded. On account of the chronic nature of tuberculous infection, the results recorded cannot be considered as the final stage in the patients' history. They serve, however, as a useful guide in the treatment of patients suffering from advanced pulmonary tuberculosis. The average period of observation was three years.

Table 39. THE END RESULTS.

Data.	Group X.		Group Y.		Group Z.	
	No.	%.	No.	%.	No.	%.
Patients alive.	22.	88.	14.	56.	19.	76.
Patients dead.	3.	12.	11.	44.	6.	24.
Artificial Pneumothorax. Maintained.	16.	64.	1.	4.	7.	28.
Abandoned.	7.	28.	24.	96.	18.	72.
Voluntarily terminated by the physician.	2.	8.	0.	0.	0.	0.
End Results. Obliterative pleuritis.	9.	36.	13.	52.	9.	36.
Serous effusion persisted and artificial pneumothorax was maintained.			0.	0.	3.	12.
Serous effusion disappeared and artificial pneumothorax was maintained.			1.	4.	4.	16.
Tuberculous empyema.			10.	40.	8.	32.
Secondarily infected empyema.			1.	4.	1.	4.
Obliterative pleuritis following empyema.			9.	81.	9.	100.
Empyema persisted.			2.	18.	0.	0.

It will be seen from table 39 that over a three year period of study, the patients in whom effusions developed were found to have a much higher mortality rate than those whose pleural space remained dry. This increased mortality rate coincided with a high percentage rate for pneumothoraces which were abandoned. It will be of interest to note the mortality rate for the patients with moderately advanced disease and for those with far advanced disease, in the three groups X, Y, and Z. It was found that no patient with moderately advanced disease died in any of the three groups. The mortality rate for patients with far advanced disease was 18.75%, 57.9% and 30% respectively for the groups X, Y and Z. All deaths were attributable to advancing bilateral pulmonary tuberculosis in group X; in group Y, the cause was similar, although hastened in two patients, (43, J.B., 47, J.B.), by tuberculous empyema; in group Z, one patient who suffered from unilateral disease died immediately following a thoracoplasty, but in the remaining five patients, death was attributable to advancing bilateral disease hastened in one patient by a tuberculous empyema. It is evident then that only in three patients could a complication of pneumothorax therapy have had any important connection with the patient's/

patient's death.

It was noted previously that the incidence of empyemata in the fifty patients comprising groups Y and Z was 22%. The mortality rate for this group of patients having empyemata was 14% whereas the mortality rate for patients in the same groups who developed serous effusions was 20%. This latter figure resulted from the high incidence of bilateral disease in these patients, and also from the relatively greater number of patients who had serous effusions alone. If one considers the patients of groups X and Y, twenty-five of whom had no effusion, the incidence of empyemata still works out at 22%, but the mortality rate rises to 45.4%. The corresponding mortality rate for patients who had serous effusions alone, is 42.8%. It is obvious from these figures that the presence of advancing bilateral disease makes a study of these statistics of little value. Burrell(149), in comparing the mortality rate in patients having serous effusions and in those having empyemata, found that the outlook was more serious when purulent fluid was present, but that the mortality rate was high in all patients who suffered from extensive disease. Brock, Mullen and Woodson (33) found that serous effusions had little to do with the cause of death in their patients, and that those who developed empyemata did not have a higher/

higher death rate than those who developed only a serous effusion. They found, as did the writer, that death was usually caused by progression of the pulmonary disease. It is well known that secondary infection of a tuberculous empyema causes a sharp rise in the mortality rate. Leaver and Hardaway(36)found a mortality rate of 22.9% for patients having pure tuberculous empyemata, whereas for those with mixed empyemata it rose to 70.9%. One of the writer's two patients who suffered from a mixed infection died, group Y (47, J.B.). The other, group Z (6, A.R.), is still alive and a sinus following thoracotomy has healed satisfactorily. She is not fit to work.

It is interesting to record that in only two patients (43, J.B.) and (47, J.B.)in group Y, and in two patients (6, A.R.) and (18, M.A.)in group Z, did empyemata fail to dry up with repeated aspiration. No air was allowed to enter the pleural cavity during or after aspiration, the negative intrapleural pressure induced by the aspiration being maintained in order to assist re-expansion of the lung. Thus, 80% of the empyemata were controlled. Salkin and Cadden(150) give a similar figure for their series of two hundred and twenty-five empyemata occurring in a series of one thousand three hundred and eighty-nine artificial pneumothoraces. Goorwitch (20) however, states that "major surgical treatment/

treatment yields and will continue to yield a higher percentage of permanently successful results than aspiration or intrapleural medication." Four patients in group Y, (15,E.W., 23,M.B.,42,M.W.,43,J.B.) were treated for a short period by the intrapleural injection of a Promanide solution, but this treatment had to be abandoned owing to the deleterious effect on thepatients' health and blood picture.

It is striking that the percentage of patients among the seventy-five under consideration who benefitted from pneumothorax treatment was 73% for the unilateral group and 49% for the bilateral group. Frimodt-Möller and Verghese (16) give 88.5% and 48.9% for the corresponding figures in their series of six hundred and ninety patients.

Eight patients of the seventy-five had thoracoplasty performed at some time after pneumothorax treatment had been abandoned. Two belong to group X (20,M.McH., 37,A.V.), four belong to group Y (10,M.McA., 29,J.W., 32,A.K., 34,A.McN.), and two belong to group Z (2,M.B., 9,H.McG.). One died immediately after operation, group Z (2,M.B.) and one has had an unsatisfactory result due to his wound repeatedly breaking down, group Y (34,A.McN.). The remaining six patients are in excellent health. Five of these cases previously had a tuberculous empyema.

Conclusions.

1. The end results of pneumothorax treatment are more favourable in patients who do not develop effusions during treatment.
2. The high mortality rate found in patients who developed effusions was due to advancing bilateral disease and not directly attributable to the effusion.
3. Tuberculous empyema is a serious complication of artificial pneumothorax which, however, can be satisfactorily controlled in many instances. Thereafter, suitable collapse measures can be applied to the lung if necessary.
4. The percentage of beneficial results obtained by patients suffering from either unilateral or bilateral pulmonary tuberculosis, still makes artificial pneumothorax a measure worthy of trial in spite of the frequency of complications.
5. Artificial pneumothorax, even although only partially successful, will sometimes so control acute disease that at a later date a successful thoracoplasty can be performed.

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